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OSTEOMYELITIS OF THE SKULL RESULTING FROM INFECTION IN THE SINUSES

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Osteomyelitis of the bones of the skull resulting from an infection in the accessory sinuses of the nose is not uncommon and has been known a long time, but Tilley [1] was the first to note such a relationship. Luc [2] reported a case at a meeting of the British Medical Association in 1897, and since that time many valuable contributions have been made. McKenzie,[3] in 1913, published the most outstanding paper in English on this subject up to that time. Previous to McKenzie's contribution there had been articles from the Continent by Schilling,[4] Gerber,[5] von Eicken,[6] Killian [7] and others. McKenzie based his discussion on the record of 48 cases of osteomyelitis of the skull resulting from infection in the sinuses and ears. This paper was remarkably complete, and little has been added to knowledge of the subject since it was written. Bulson,[8] in 1925, published a complete review of osteomyelitis of the frontal bone and brought the literature up to date, recording a total of 55 cases, in 37 of which the disease ended in death. Reports of cases have also been made by Lillie,[9] Dabney,[10] Hastings,[11]

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1. Tilley, H.: A Fatal Case of Chronic Frontal Sinus Empyema, Lancet **2**: 534, 1899.

2. Luc, H.: A Fatal Case of Frontal Sinus Empyema, Lancet **2**:461, 1899.

3. McKenzie, D.: Diffuse Osteomyelitis from Nasal Sinus Suppuration, J. Laryng. **25**:128, 1913.

4. Schilling, R.: Ueber die Topographi der Diploe im Stirnbein, und über die Osteomyelitis der flachen Schädelknochen, Ztschr. f. Ohrenh. **48**:52, 1904.

5. Gerber, P. H.: Die Komplikationen der Stirnhöhlenentzündungen, Berlin, S. Karger, 1909.

6. von Eicken, C.: Meningitis bei Stirnhöhlenentzündung, Ztschr. f. Laryng., Rhin. **18**:340, 1929.

7. Killian: Die Thrombophlebitis des oberen Langsblutleiters nach Entzündung der Stirnhöhlenschleimhaut, Ztschr. f. Ohrenh. **38**:343, 1900.

8. Bulson, A. E., Jr.: Osteomyelitis of Frontal Bone as a Complication of Frontal Sinusitis, J. A. M. A. **86**:246 (Jan. 23) 1926.

9. Lillie, H.: Osteomyelitis of Skull Secondary to Paranasal Sinus Operations, Ann. Otol., Rhin. & Laryng. **34**:353, 1925.

(Footnotes continued on next page)

Shea,[12] Woodward,[13] McKinney [14] and others. All of these have added to present knowledge of the subject. Within the last few years the literature has been greatly enriched by the papers of Furstenberg [15] and of Mosher and Judd.[16]

ETIOLOGY

Bulson [17] cited Luc [18] as saying that in his opinion cranial osteomyelitis occurs only in persons presenting a developmental anomaly.

Sex.—Some authors have reported a marked preponderance of females over males, while others have found little variation between the sexes.

Age.—Tables of reported cases show that before the age of 10 years osteomyelitis of the bones of the skull rarely develops as a result of infection of the frontal sinus. As there is practically no frontal sinus up to the fourth year of life and as it is small for several years thereafter, one could not expect to see this complication arise from the frontal sinus during this period except in rare instances, but it might arise from infection in the ethmoid cells, the antrum or possibly the sphenoid sinus. Most of the patients are seen when they are between the ages of 20 and 30 years. It has been said that this is the period during which most of the operations on the frontal sinuses are done, but in my opinion this has little bearing on the subject. Many operations on the sinuses are also done on patients between the ages of 30 and 50 years; yet comparatively few infections in the bones of the skull take place during this period. The older the patient, the denser the walls of the frontal sinus and the less is the amount of diploic

10. Dabney, V.: Osteomyelitis of the Frontal Bone, Arch. Otolaryng. **8**:177 (Aug.) 1928.

11. Hastings, H.: Acute Fulminating Osteomyelitis of the Frontal Sinus, Arch. Otolaryng. **6**:559 (Dec.) 1927.

12. Shea, J. J.: Osteomyelitis of Frontal Bone: Two Cured Cases, Tr. Am. Laryng., Rhin. & Otol. Soc. **34**:395, 1928.

13. Woodward, F. D.: Osteomyelitis of Skull: Report of Cases Resulting from Frontal Sinus Infection with Staphylococcus, J. A. M. A. **95**:927 (Sept. 27) 1930.

14. McKinney, R.: Osteomyelitis of Frontal Bone: Report of Eight Cases, Arch. Otolaryng. **28**:1 (July) 1938.

15. Furstenberg, A. C.: Osteomyelitis of the Skull: The Osteogenetic Processes in the Repair of Cranial Defects, Ann. Otol., Rhin. & Laryng. **40**:996 (Dec.) 1931.

16. Mosher, H. P., and Judd, D. K.: An Analysis of Seven Cases of Osteomyelitis of the Frontal Bone Complicating Frontal Sinusitis, Laryngoscope **43**: 153 (March) 1933.

17. Bulson, A. E., Jr.: Osteomyelitis of the Frontal Bone as a Complication of Frontal Sinusitis, Tr. Am. Acad. Ophth. **30**:117, 1925.

18. Luc, H.: Complications craniennes et intracraniennes des antrites frontales suppurées, Ann. d. mal. de l'oreille, du larynx **35**:265, 1909.

bone surrounding the frontal sinus. It seems to me that the larger the frontal sinus, the more severe the infection and the less satisfactory the treatment of the sinusitis, the greater the danger of osteomyelitis.

Site of Origin.—It is not difficult to visualize how the frontal sinus, with its long, tortuous duct and poor drainage, is more likely to be the source of an infection extending upward to the bones of the skull than the antrum, with its membranous nasal wall and direct opening into the nose. As far as the opening is concerned, the same line of reasoning could be applied to the ethmoid cells and the sphenoid sinus. There is diploic bone at the junction of the anterior and the posterior wall of most frontal sinuses, and it may surround a considerable part of the sinus. The latter statement can also be made about the sphenoid sinus.

In practically all cases osteomyelitis of the skull originates from the frontal sinus and in very few from the ethmoid cells or the antrum. It is my belief that osteomyelitis arises from infection in the sphenoid sinus in many more cases than are reported in the literature. In a large percentage of cases in which the osteomyelitis arises from infection of the sphenoid sinus the condition is discovered at the autopsy table.

It has been said that osteomyelitis of the skull may arise during either acute or chronic infection, but I presume almost all observers agree that an acute exacerbation of chronic sinusitis is necessary to cause extension to the bony walls of the sinuses or to the vascular channels, with extension to the surrounding bone. Local destruction of bone, however, can take place with few, if any, acute manifestations.

Infectious Diseases.—Sinusitis arising during the course of influenza, a common cold, scarlet fever, measles and other infectious diseases is the usual precursor of osteomyelitis of the skull. In many cases swimming, with chilling of the body from long exposure, as emphasized by Taylor,[19] has been observed as an etiologic factor.

Operative Procedures.—Osteomyelitis of the skull has been described as developing spontaneously or after an operative procedure on the sinuses. Some authors have reported that in about one half of their cases the disease developed as a result of an operative procedure. Others have reported a much smaller incidence of this postoperative complication, but all emphasize operative procedures as being an important factor in the causation of osteomyelitis of the skull complicating sinusitis. I have seen only 1 case of osteomyelitis of the skull associated with an operation on the sinuses. This was osteomyelitis of the skull with abscess of the brain following a complete ethmosphenofrontal operation which was performed during a slight exacerbation of chronic sinusitis. The acute infection was not suspected before the procedure was begun. The wound was entirely closed

19. Taylor, H. M.: Sinusitis and Swimming, J. A. M. A. **85**:7 (July 4) 1925.

externally, and the abscess in the brain formed without any one's having recognized the presence of osteomyelitis.

It has been said that osteomyelitis may arise after even a very minor operation, as well as after a more extensive procedure. It has always seemed to me that if the operator would remember that only drainage is to be instituted in cases of acute sinusitis, the incidence of the complications, including osteomyelitis of the skull, would be much lessened. It should also be remembered that opening the frontal sinus through the anterior wall, instead of entirely through the floor, may be a cause of osteomyelitis. In operating on any of the sinuses, especially the frontal, one cannot be too careful in handling the tissues, particularly the bone. The vigorous use of the curet or any use of the rasp is contraindicated. In all my cases, with 1 exception, the disease arose spontaneously and had no connection whatever with any operation.

Osteomyelitis is usually described as an extension of an infection in the frontal sinus by directly involving the bony walls, especially the diploe of the bone, and then by continuous involvement of the bone surrounding the sinus, more often in an upward and lateral direction. Some authors have described this osteomyelitic process as arising through implication of the veins of the mucous membrane of the sinus, usually thrombophlebitis, with direct extension to the diploic veins of the skull. The usual veins involved are the frontal diploic or the anterior temporal diploic vein. From these veins the infection may extend through emissaries to the longitudinal sinus and then to the meninges, to the brain proper or to a distant part of the brain. It must be remembered, though, that by direct extension any region surrounding the frontal sinus may be involved. In the sphenoid sinus the infection usually takes place through the roof and the basilar process, the patient dying of meningitis and the osteomyelitis being overlooked until the postmortem examination.

BACTERIOLOGY

The staphylococcus is the offending organism in most cases of osteomyelitis of the skull, but occasionally streptococci or other bacteria may be observed.

PATHOLOGY

Gross Changes.—In the early stages the bone looks almost normal to the naked eye. Following this stage there are pronounced engorgement of the vessels of the diploe and the formation of pus in the interspaces. Abscesses in the bone, with formation of granulation tissue, are to be seen at this period. Thrombosis of the vessels may occur early and continue to the end stage. The thrombosis may be in advance of the bone suppuration, depending on the type and rapidity and extension of the disease. Purulent secretion extends to the inner

or outer surface of the bone, either by direct extension or through the vessels. Furstenberg [20] stated: "The inner table is more often affected than the outer."

After the rupture through the outer table of the skull, there may be a subperiosteal abscess and swelling of the periosteum and soft tissues, giving the puffiness that is so well known as a symptom of osteomyelitis. These soft tissues may break down and drain externally. If, as is more common, the infection extends inwardly, an epidural abscess, with formation of granulations on the dura, is often seen. The dura is fairly resistant, and there may be no extension through it. Occasionally, however, there is involvement of the subdural space with abscess formation, or an abscess of the brain may form directly under the osteomyelitic process by direct extension or through thrombosis of veins. or in a distant area on the same side or even in the opposite hemisphere of the brain.

In the early stages of the disease the appearance of the bone shows little change from the normal, but later it may be perfectly white with little, if any, tendency to bleed. As it breaks down it appears worm eaten, or as if corroded with acid. Later large openings are seen in the cortex with discoloration of the bone. The involvement of the bone may be localized, or there may be several areas of destruction with comparatively good bone between. Fibrosis and new bone formation are not uncommon, but the usual changes are those of destruction.

Microscopic Changes.—In the complete ethmosphenofrontal operation, I have for several years made it a practice to take a portion of the bone and mucous membrane from each sinus for microscopic study; invariably, even though the condition was chronic and in a quiescent stage, there were many signs of active osteomyelitis in practically all specimens. There were osteoclasts, with destruction of bone, and abscesses in the medullary spaces, showing active inflammation, as well as osteoblasts and formation of fibrous tissue. One can easily visualize how this condition may be changed into an active, spreading inflammatory process.

As already stated, I have seen only 1 case of fulminating osteomyelitis associated with an operative procedure on any sinus. The early changes in the bone marrow are the presence of bacteria with round cell infiltration of the medullary spaces, while abscess formation is not uncommon.

Osteoclasts soon make their appearance in the bone. Blood vessels may be thrombosed; and if the process is very acute the thrombosed area may become abscessed; if it is more chronic, the area becomes localized and changes to scar tissue.

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20. Furstenberg, A. C.: Osteomyelitis of the Skull: The Osteogenetic Processes in the Repair of Cranial Defects, Ann. Otol., Rhin. & Laryng. **40**:1603 (Dec.) 1931.

TYPES OF OSTEOMYELITIS

Osteomyelitis is sometimes divided into the localizing and the spreading form, which may be fulminating. Some authors, in speaking of localizing osteomyelitis, say that it is benign with little, if any, tendency to spread, while the spreading type may be described as an entirely different condition with a bad prognosis. All observers recognize the fact that in one case the disease may be comparatively benign while in another it may be lightly malignant, but it seems to me that the dividing line is indefinite and that the localizing type may become fulminating and progressive, depending on the resistance of the patient, the virulence of the infection and the form of treatment, or that what starts as a fulminating type may end spontaneously. Certainly any one who has followed a reasonable number of patients with this condition has seen what seemed to be a minor, localized condition change to a fulminating, progressive type while the patient was under treatment. I am convinced that the sooner one learns that there is no definite dividing line between the two types and that one should be alert in all procedures of treatment, the better the prognosis will be.

The usual pathologic complications observed are: subperiosteal abscess; abscess in the soft tissues over the bone, as well as subdural abscess; abscess of the brain; thrombosis of the intracranial sinuses, and meningitis.

SYMPTOMS AND COURSE

Osteomyelitis of the skull may result from infection of any of the sinuses, but in the usual case it arises from infection in the frontal sinus. There is usually a history of a rather severe infection of the frontal sinus, with more than the usual amount of pain and tenderness and unsatisfactory intranasal drainage.

One should not forget the history of previous operations, of swimming and of infectious diseases and their relation to the nasal symptoms. The first symptoms to be noticed may be swelling of the frontal region, closure of the eye associated with pain in the sinus, etc., which may indicate only periostitis or rupture of the frontal or sinus ethmoid, but may also denote beginning extensive osteomyelitis of the skull. The temperature may vary from normal to 103 or 104 F., depending on the acuteness and the extent of the condition. It is not unusual to have extensive osteomyelitis of the skull with no history whatever of high temperature or of pronounced symptoms of involvement of the frontal sinuses, but in practically all cases there is a history of sinus infection and examination of the nose will almost invariably show an acute or subacute infection in the frontal or other sinuses. At times the symptoms referable to the sinuses are so mild and the infection has become so quiet that sinusitis is overlooked.

In practically all cases of osteomyelitis of the frontal region there is a puffy swelling which is indicative of this condition and should not be overlooked. Mosher and Judd [21] noted the importance of this edema of the soft tissues and emphasized that it usually extends 1½ to 2 inches (3.8 cm.) farther peripherally than is evident in roentgenograms and that the edema is a good guide to the limit of the infection in the bone marrow. The roentgenogram will always show increased density of the sinus, but in early stages the roentgenogram of the frontal region will not be positive, as the decreased density, with absorption or destruction of the bone, will be present only after necrosis of the bone has taken place.

In some cases the disease lasts only a few weeks, while in others it extends over a period of several months. Some patients have active symptoms through the entire course, while others have periods of quiescence, especially between operative procedures. At times the quiescent period may cause one to think the condition has healed, but later symptoms of further extension arise. One patient may never appear to be very sick and may recover in a few weeks, while another may be critically ill from the beginning to the end of the disease and also recover after having had one or all of the complications. Of course, the symptoms would vary greatly between the two conditions. In the benign type the temperature may be practically normal and there may be few general symptoms, while in the acute fulminating type the temperature is high and the patient toxic. Redness of the skin, simulating erysipelas, and abscesses of the soft tissues of the frontal region are not uncommon. Rigor is not unusual. Since general symptoms would be altered by the presence of complications, such as subperiosteal abscess, abscess of the soft tissues of the frontal region, epidural abscess, subdural abscess, abscess of the brain and meningitis, they will not be discussed further.

PROPHYLACTIC TREATMENT

Prophylactic Therapy.—Prevention of Sinusitis: One of the more important steps in the prevention of sinusitis is probably, as Taylor [22] said, "the control of the swimmers and the pool." Diving is always detrimental to the nasal passages. Long periods of swimming, with chilling of the body, should be discouraged. Correction of nasal deformities and removal of growths, such as the adenoids and tonsils, should

21. Mosher, H. P., and Judd, D. K.: An Analysis of Seven Cases of Osteomyelitis of the Frontal Bone Complicating Frontal Sinusitis, Laryngoscope **43**:211 (March) 1933.

22. Taylor, H. M.: Otitis and Sinusitis in the Swimmer, J. A. M. A. **113**:891 (Sept. 21) 1939.

not be overlooked. Proper treatment of infections of the nose during acute infectious diseases should be emphasized.

Prevention of Osteomyelitis After Sinusitis: I shall not attempt in this paper to give the different treatments that may be carried out after sinusitis has already developed, but I do want to emphasize the importance of treatment, especially in cases of the chronic type in which an operative procedure is necessary. Such a procedure should be carried out only in a quiescent period, and if there is an acute attack of sinusitis no operation except drainage should be performed. In my opinion, the employment of any intranasal surgical procedure except drainage in the presence of acute infection of the sinuses would be extremely dangerous. But to sit quietly by in a case of acute fulminating infection of a sinus, especially of the frontal, and allow it to rupture, with or without complication, such as meningitis or osteomyelitis of the skull, is not treatment of which one could be proud.

In cases of suppuration of the middle ear with moderate pneumatization of the mastoid, severe pain in the ear and head, considerable loss of hearing and swelling of the posterior and superior canal walls, the otologist does not usually wait until there is a subperiosteal abscess, meningitis or sinus thrombosis before he suggests drainage of the mastoid. I doubt whether there is much more reason for a continued period of waiting in a case of infection of the frontal sinus than there is in the case of infection of the mastoid. It seems to me that drainage of the frontal sinus in adults, or of the ethmoid sinus in children, should not be an operation of last resort. If there are noticeably increased density of the frontal sinus with a history of suppuration, pronounced tenderness of the frontal region and poor intranasal drainage, signs which indicate unsatisfactory progress, extranasal drainage through the floor of the frontal or the ethmoid sinus should be carried out. Certainly, if there is external swelling with closure of the eye, accompanied by the signs previously described, immediate external opening of these sinuses is indicated. The intranasal procedure in the presence of these signs and symptoms would be dangerous, and to employ it would be courting complications, such as meningitis and osteomyelitis. If the external procedure is carefully carried out, with the institution of drainage only, there is practically no danger of further extension of the disease.

The procedure which has become somewhat routine is as follows: In adults, under such analgesia as that induced with scopoline and morphine, or whatever drug the surgeon may favor, and local anesthesia, a curved incision is made well below the eyebrow. This incision need not be more than ¾ inch (1.9 cm.) long. The incision extends through the periosteum. The periosteum is elevated laterally from the line of incision, which uncovers the floor of the frontal sinus and the

anterior ethmoid cells, and with an Alexander gouge an opening is made and enlarged with biting forceps. In this manner the frontal sinus and the anterior ethmoid cells are both opened. Drainage is carefully carried out by the insertion of a small rubber tube into the frontal sinus and the placing of another between the middle turbinate and the lateral wall of the nose through the ethmoid cells. The mucous membrane of the frontal sinus is not disturbed. No curettement of any kind is done. In this manner the frontal sinus and the ethmoid cells are drained. No further operative procedures are carried out at this time. The drainage tubes can be left in the wound from two to five days, depending on the course of the sinusitis. The wound is then allowed to close, no sutures being necessary.

In children, under general anesthesia, with the same incision as that already described, an opening is made through the lamina papyracea and the ethmoid cells are drained, a single rubber tube being placed between the middle turbinate and the lateral wall through the ethmoid.

These procedures have been satisfactory and resulted in no complications. I have not seen a single case of osteomyelitis of the skull develop after this operation. The complete ethmosphenofrontal operation should never be done when the disease is in the acute stage, no matter how extensive the disease. If such an operation is indicated, it should be carried out only after the condition has become quiet, usually after an interval of several months.

Treatment of Osteomyelitis.—I shall not discuss in detail the treatment of osteomyelitis, as each surgeon must decide the best procedure to be instituted in each case. In my opinion, whether one uses the median line or the coronal suture incision is of little moment, for this decision must be left in each case to the surgeon. It seems to me that the crux of the situation, which has been so often discussed since the work of McKenzie,[3] is the entire removal of all diseased bone without trauma to the surrounding tissues and the proper handling of any complication which may have arisen. As has been emphasized by Mosher,[23] to be sure that all diseased bone has been eradicated, one should remove all bone from 1.5 to 2 inches (3.81 to 5.08 cm.) beyond the necrotic area which is visible to the naked eye. At the time of the operative procedure on the osteomyelitic focus, removal of the floor of both frontal sinuses with exenteration of the entire mucous membrane of these cavities may be carried out, or if the condition is acute and the patient seriously ill, the exenteration of the sinuses can be done one to two weeks later but should be performed while the wound in the frontal sinus is open; this facilitates very much the exenteration of all mucous

23. Mosher, H. P.: Osteomyelitis of the Frontal Bone as a Complication of Frontal Sinusitis, J. A. M. A. **115**:1179 (Oct. 5) 1940.

membrane from all parts of the frontal sinuses. This procedure usually prevents subsequent infections in the frontal sinuses, with extension to the bones of the skull.

PROGNOSIS

The prognosis varies, depending on the virulence of the infection, the type of osteomyelitis and the operative procedure. If the osteomyelitis is seen at its beginning and the correct operative procedure is carried out, the prognosis will be much better than if the patient is seen late, after such complications as abscess of the brain or thrombosis of a cranial sinus have arisen. The prognosis has become better within the last few years, since the operative procedures have been improved and the use of sulfanilamide and its derivatives has come into vogue.

REPORT OF CASES

A report of 18 cases of osteomyelitis of the skull resulting from infection in the accessory nasal sinuses follows.

CASE 1.—J. G., a boy 14 years of age, gave a history of scarlet fever six weeks previously and severe pain and swelling of the right frontal region, with closure of the right eye, four weeks before. Two days later external drainage of the right frontal sinus was instituted by another surgeon.

When I first saw the patient, there was moderate swelling of the right frontal region and the right eyelids, with a fistula through the skin leading into the frontal sinus. Through this fistula considerable roughened bone could be felt.

With the patient under ether anesthesia, an ethmofrontal operation was done on the right side. The ethmoid cells were filled with swollen polypoid mucous membrane. The middle turbinate was left intact. Practically the entire floor of the frontal sinus had been removed at the previous operation. The sinus was filled with pus and granulations, and the mucous membrane was acutely swollen. The bone of the anterior wall of the sinus seemed to be very rough, as though there had been no mucous membrane on it. There were five sequestrums of the posterior wall of the frontal sinus, under which area a portion of the dura about the size of a dime was exposed. The dura seemed to be normal. The wound was left open and was packed with iodoform gauze.

The patient made an uneventful recovery.

CASE 2.—Mrs. T. W. M., aged 65, gave a history of sinus trouble for many years, with many acute attacks. The present attack began five weeks previously. She had severe pain over the left eye, with redness and swelling of this region. On the fifth day there was a rupture through the skin of the upper lid toward the outer canthus, and a rubber tube drain was placed in this fistula by her physician.

Examination revealed a fistula which led upward and inward through the upper lid near the outer canthus into a cavity containing pus. Roughened bone could be felt. A roentgenogram showed considerably increased density of all the sinuses. There was a rather large area of decreased density far to one side in the frontal region.

With local anesthesia, an external ethmosphenofrontal operation was performed on the left side. The frontal sinus was filled with granulations and mucopus. The

bone was very rough. A moderate-sized supraorbital ethmoid cell was surrounded by thick bone, which was badly diseased, soft, vascular and somewhat necrotic. This area extended laterally as far as the temporal fossa but not into it. There was an extension of this cavity posteriorly over the medial part of the orbit, which was surrounded by thick, somewhat diseased bone. The fistula through the upper lid in the region of the outer canthus led into this ethmoid cell, which was surrounded by osteomyelitic bone. Nearly complete exenteration of this ethmoid space was done through an external incision from the fistula of the upper lid. The ethmoid cell extended laterally well beyond the frontal sinus. The entire floor of the frontal sinus and all the bone between this cavity and the ethmoid cell were removed. The remaining ethmoid cells and the sphenoid sinus were badly diseased, and exenteration was carried out.

The patient made a rapid and satisfactory recovery.

CASE 3.—C. J., a boy 10 years of age, had a history of scarlet fever.

Examination revealed slight swelling of the tissue over the left frontal sinus and the lids of the left eye. There was slight tenderness of the frontal region. He was given ephedrine, and on the following day the swelling was about gone and the tenderness was much less. Conservative measures had been carried out for five days, when the left eye again became swollen.

A roentgenogram showed pansinusitis on the left side, with a rather large area of decreased density in the anterior wall of the frontal sinus.

With the patient under ether anesthesia, the left frontal sinus was opened. The periosteum was gone from the floor and the entire anterior wall of the sinus. There was a rather large opening through the bone on the anterior wall. The bone was rough over the entire anterior wall and the floor (roof of the orbit). The mucous membrane of the sinus was necrotic, and most of it was detached and lay loose in the cavity. The cavity was full of pus and granulations. The entire floor and the anterior wall were removed. The sinus was packed with iodoform gauze.

The patient made an uneventful recovery.

CASE 4.—C. P. D., a man aged 41, had a history of bilateral pansinusitis and osteomyelitis of the frontal bone. Several operations had been performed on the frontal region and several pieces of bone removed previous to his coming under my care. Marked swelling and redness were evident in the frontal region, with a fistulous tract in the median line from which pus was exuding. There was a localized swelling of this region, which became larger after he blew his nose. The latter condition dated from the first operation on the bone in this region. Pressure on this localized area caused air to escape into the nose and the mass to become smaller. The area could be reinflated by blowing the nose. A roentgenogram of this region showed severe destruction of bone.

Several operations were done on the sinuses, and considerable bone of the frontal region was removed, with a final satisfactory result and no further trouble.

CASE 5.—Mrs. M. Q., aged 55, gave a history of severe headaches and dizziness eighteen years previously, which condition was relieved by a radical external operation on the right frontal sinus. There had been recurrence of pain during the last six months, with swelling of the region of the right eye and formation of a fistula in the right ethmoid region.

A roentgenogram showed increased density of all sinuses, with chronic osteomyelitis of the frontal bone.

The usual Lynch incision was made, with the use of local anesthesia. The frontal sinus and the ethmoid cells were found to be extensively diseased on the

right side. The frontal sinus was partially obliterated, but the remainder of the space was lined with a much thickened mucous membrane. Considerable necrotic bone was removed from the medial and posterior walls of the frontal sinus.

An uneventful recovery was made.

CASE 6.—M. E. B., a girl aged 13 years, had a history of severe frontal headaches for five days, with some swelling around the eyes, especially the right. She had been unconcious for two days.

Examination showed swelling of all the turbinates, stoppage of the nasal passages and considerable yellow pus on both sides. The eyegrounds were normal. Roentgenograms showed increased density of all the sinuses.

With the patient under ether anesthesia, external drainage of the ethmoid and frontal sinuses on both sides was established, with simple drainage of the antrums. There was much pus in all the cavities, especially the left frontal sinus. In twenty-four hours the patient became conscious. Six weeks later there was swelling of the left frontal region. A roentgenogram showed an extensive area of decreased density

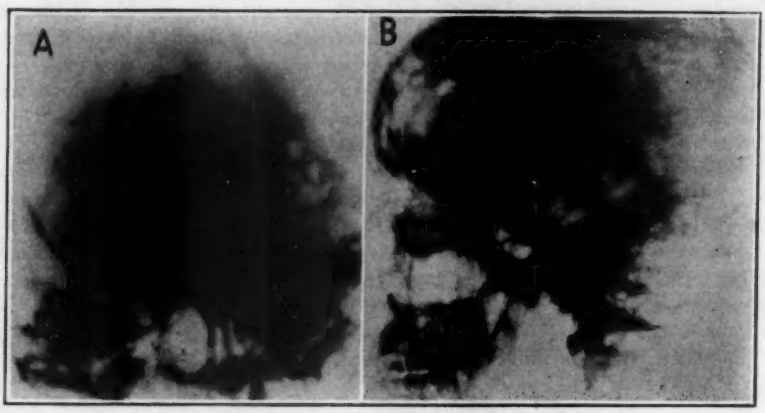

Fig. 1 (case 6).—*A*, anteroposterior, and *B*, lateral, view, showing osteomyelitis of the left frontal region.

in the left frontal region above and to the left of the frontal sinus. Dr. Francis Murphey, of the neurosurgical division, performed an operation on the region, in which he encountered necrotic bone and an abscess of the left frontal lobe.

The patient had a satisfactory convalescence.

CASE 7.—H. S., a Negress aged 23, gave a history of a blow on the left frontal region two months previously. There had since been pain, swelling and tenderness in this region just above the eyebrow, which symptoms gradually became more severe.

Examination showed moderate swelling, redness and tenderness of the left frontal region and the upper lid of the left eye, especially toward the outer canthus. Roentgenograms revealed mottling of the left frontal bone, which was suggestive of early osteomyelitis.

With the use of local anesthesia, a horizontal incision was made ½ inch (1.3 cm.) above the left eyebrow, extending from almost the median line externally for 3 inches (7.6 cm.). The bone of the left frontal sinus was rough and worm eaten, some of the depression being filled with granulations. As the periosteum

was lifted from the rim of the orbit, about 2 drachms (7 cc.) of yellow pus came from the roof of the orbital region. In no place was the entire thickness of the bone removed, and the dura was not exposed. The wound was packed with iodoform gauze.

Recovery was uneventful.

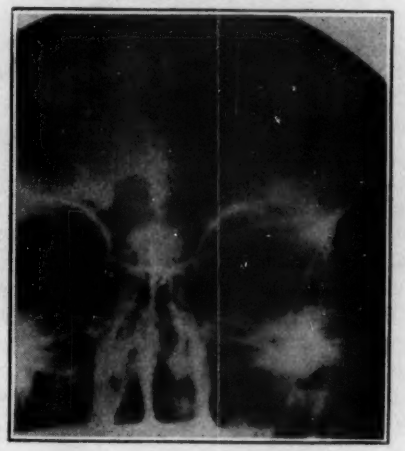

Fig. 2 (case 8).—Roentgenogram, showing osteomyelitis of the right frontal bone.

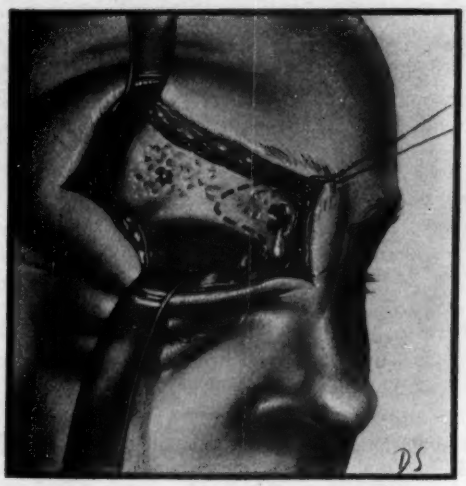

Fig. 3 (case 8).—Drawing of operative field in the right frontal region.

CASE 8.—J. G., a boy aged 14 years, had a history of having been hit on the head by a baseball one month previously, when he had been unconscious a short time. He had been swimming during the season, the last time one week

after being injured by the baseball. There was a history of severe frontal headaches, swelling of the right eye and vomiting, starting five days before admission.

Examination.—The right eye was closed. There was moderate swelling of the right frontal region. Pus was present in the right side of the nose. A roentgenogram showed pathologic changes in the right antrum, but no mention was made of any alteration in the right ethmoid cells or the right frontal sinus, and no fracture lines were seen.

With the patient under general anesthesia, an external incision was made into the right orbit, and a large abscess which extended over the entire right frontal region was evacuated.

Treatment with sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) was ordered.

Three weeks later a roentgenographic study was made. Stereoscopic examination of the frontal bone showed a large destructive lesion around the right frontal sinus and above it, involving a large portion of the right frontal bone.

The wound in the right frontal region was reopened, and the entire anterior wall of the frontal sinus was removed. The cavity was packed with iodoform gauze. The bone of the anterior wall of the sinus was worm eaten and soft, and there was an opening through the anterior wall.

The patient became gradually worse, and Dr. Eustace Semmes, chief of the neurosurgical division, removed the bone of the entire right frontal region and drained a large abscess of the frontal lobe.

The patient died.

CASE 9.—P. W., a man aged 24, gave a history of a discharge from the nose for three years. The patient had been swimming and diving three weeks prior to examination, and the discharge from the nose had become more profuse. Swelling of the left eye had been present a few days.

Examination revealed slight swelling of the frontal region, especially high above the brow, and extreme tenderness of the entire frontal area. A roentgenogram showed increased density of all the sinuses. There was a fluid level of pus in both frontal sinuses, which were poorly outlined. The bone, especially above the frontal sinuses, showed slight signs of osteomyelitis.

With the use of local anesthesia, external drainage of the ethmoid and frontal sinuses was established bilaterally. There was considerable mucus in the right frontal sinus but no yellow pus. Much creamy, yellow pus was obtained from the left frontal sinus. The usual drainage tubes were inserted into each frontal sinus.

The patient did moderately well but continued to have considerable headache. Ten days later a roentgenogram showed osteomyelitis of the left frontal region.

With local anesthesia, a horizontal incision was made about 1 inch (2.5 cm.) above the brow, more to the left side than to the right. As the periosteum was lifted off, 3 or 4 drops of mucopus was noted between the bone and the periosteum at the upper border of the frontal sinus about ¾ inch (2 cm.) to the left of the median line, the pus coming from an opening extending into the frontal sinus. There was slight roughness of the bone surrounding this area. The major portion of the anterior wall of both frontal sinuses was removed through the incision. The bone of the posterior wall of the left frontal sinus was white and was not covered with mucous membrane over an area about 1 inch (2.5 cm.) in the vertical and about 1½ inches (3.8 cm.) in the horizontal diameter. This area reached almost to the upper extremity of the left frontal sinus. At the upper extremity of this sinus, and well to the left of the cavity, a sinus led through the bone and into the subdural space. Through this sinus yellow pus was flowing. At this stage of the operation, Dr. Eustace Semmes, chief of the neurosurgical division, removed

a major portion of the white, uncovered bone of the posterior wall. About 2 ounces (60 cc.) of pus was evacuated from the subdural space. A drain was inserted in this region and the wound closed with silk sutures.

Fig. 4 (case 9).—Drawing of operative field before the sinus was opened, showing osteomyelitis.

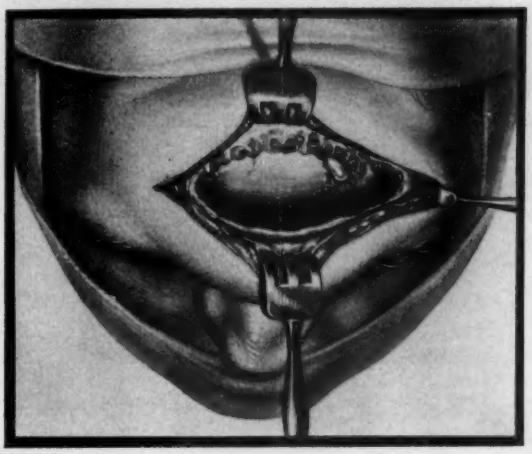

Fig. 5 (case 9).—Drawing of the operative field, showing the frontal sinuses opened and pus coming from the epidural space.

The patient was seen over a period of several months. There was considerable drainage through the cutaneous wound for several weeks but no further extension of the osteomyelitic process.

CASE 10.—J. C. F., a man aged 68, gave a history of postnasal discharge for eight months and a dull pain over the left eye. The doctor in charge of the patient had tapped the left frontal region six times with a hypodermic needle, withdrawing pus each time.

Fig. 6 (case 10).—Drawing of operative field in the left frontal region, showing exposure of the dura.

Fig. 7 (case 11).—Roentgenogram, anteroposterior view, showing extensive osteomyelitis of the entire frontal region.

Examination revealed pus in the left middle meatus. There was slight swelling of the left frontal region, especially in the region of the floor of the sinus. A roentgenogram showed a small right frontal sinus and what appeared to be a moderate-sized left frontal sinus, which was poorly outlined.

With local anesthesia, an external ethmosphenofrontal operation was performed on the left side. The usual frontal incision was made, which opened into a cavity

in the left frontal region without going through a bony wall. The entire left frontal space was filled with a mass of granulation tissue, which was easily removed. The entire bony floor and part of the anterior wall, especially toward the rim of the orbit, and about one half of the posterior wall were absent, the dura being exposed on the posterior wall. The junction of the anterior and the posterior wall was unusual, the walls seeming to be two entirely distinct pieces

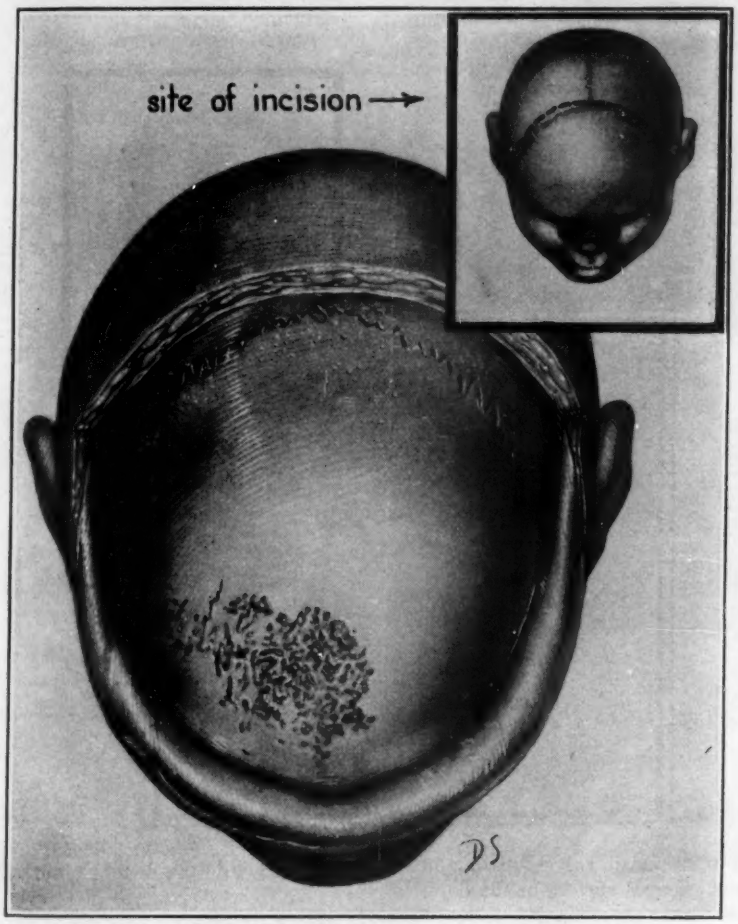

Fig. 8 (case 11).—Drawing of operative field, showing osteomyelitis of the surface of the bone.

of bone coming together, the one on the posterior wall being somewhat whiter than the one on the anterior wall. The external wound was left entirely open, and the cavity was filled with iodoform gauze.

The patient made an uneventful recovery.

Case 11.—E. H., a Negro boy 15 years of age, gave a history of having had a temperature varying from normal to 102 F. for four weeks. A diagnosis of malaria was made by the home physician, and the patient was given quinine. He was in

bed most of the time. The patient had gone swimming all summer. He had lost about 15 pounds (6.8 Kg.) in weight, and there was a continuous discharge from his nose.

A few hours before coming to the hospital he had several convulsions, for the first time in his life. These convulsions lasted from ten to thirty minutes, being of a generalized clonic type. He did not speak after the first convulsion.

Examination.—The patient was entirely unresponsive. He did not talk except when forced to inhale ammonia; then he fought and began talking. The results

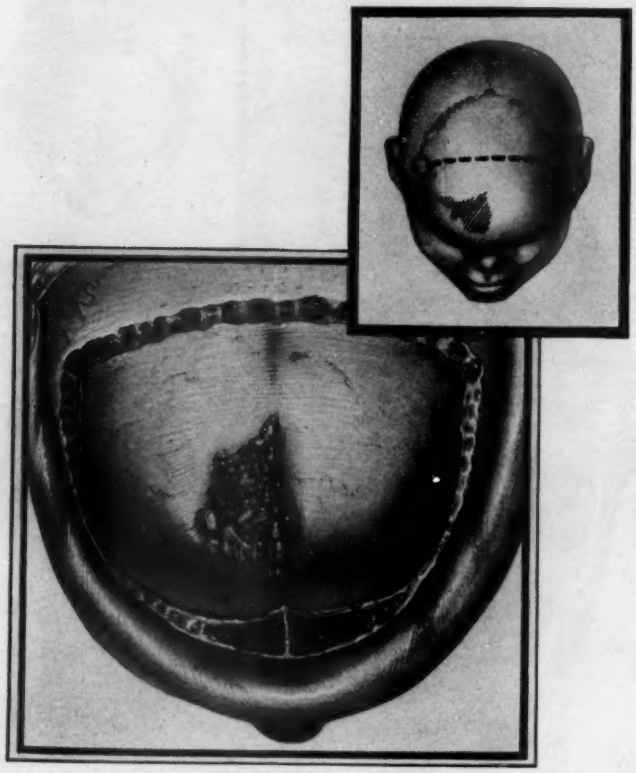

Fig. 9 (case 11).—Drawing of operative field, showing pathologic condition of the external surface of the dura.

of neurologic examination were all negative. A roentgenogram showed considerable increase in density of both frontal sinuses. Irregular, moth-eaten areas of destruction in the frontal bone, indicating osteomyelitis, surrounded the frontal sinuses and extended approximately 2 inches (5 cm.) beyond them. Sulfanilamide was prescribed.

External drainage of both frontal sinuses was instituted. Each sinus was filled with mucopus. Two weeks later Dr. Nicholas Gotten, of the neurosurgical division, made a coronal suture incision, uncovered the entire frontal and parietal regions and removed a large sequestrum of infected bone in the midfrontal region, including the anterior and posterior walls of the frontal sinuses. There was considerable granulation tissue between the bone and the dura. Rubber tube drain were inserted.

The patient made a good recovery after the removal of the osteomyelitic bone and two weeks later a complete bilateral external ethmosphenofrontal operation was done. Six weeks later the patient complained of severe headache and nausea. He had a generalized convulsion, lasting two and one-half minutes, with no loss of consciousness. One hour later his face began twitching, and he had a clonic convulsion of the left upper extremity, lasting approximately three minutes. Lumbar puncture at this time showed a cell count of 220 cells per cubic millimeter, with a spinal fluid pressure of 300 mm.

The department of neurosurgery stated that there was no evidence of abscess of the brain. The department of ophthalmology reported the presence of bilateral choked disks. Two days later Dr. Nicholas Gotten drained a large abscess of

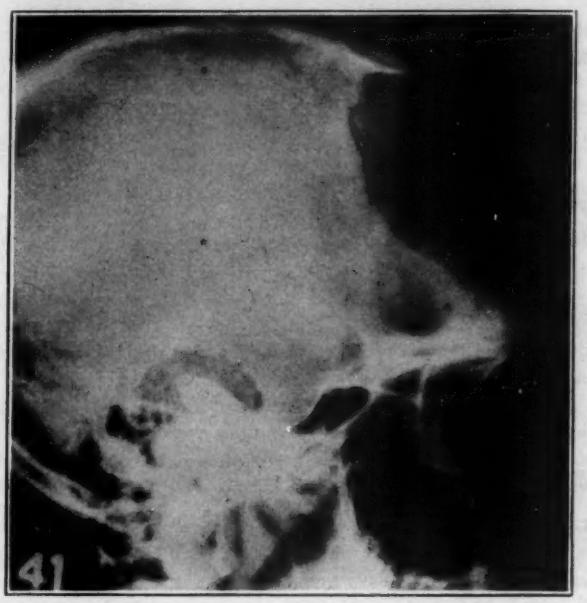

Fig. 10 (case 11).—Roentgenogram, lateral view, showing regeneration of bone.

the right frontal lobe, and ten days later a large rubber tube drain was placed in the abscess.

The patient has convalesced satisfactorily, without further symptoms.

CASE 12.—Mr. H. A. K. gave a history of scarlet fever three years previously, with infection of the right frontal sinus. An external operation on the right frontal sinus was performed, with little relief, and pus had continued to drain through the line of incision since that time. One year later a second external operation was done on the frontal sinus, after which the lid of the right eye had been retracted upward. The third operation of the right frontal sinus was done three months later, at which time some bone was removed from the sinus, but pus continued to drain through the line of incision. One year later a fourth operation was done on the same sinus. More bone was removed, and plastic repair of the upper lid was carried out.

Examination revealed a depressed scar in the region of the right frontal sinus, with marked retraction of the upper lid and a fistula at the apex of the retraction,

through which yellow pus was exuding. Vision was 20/30 in the right eye and 20/20 in the left eye. Double vision was present, and there was a history of the latter condition's being present for many months.

With local anesthesia, an ethmosphenofrontal operation was performed on the right side. Much granular mucous membrane and tissue was noted in the right frontal sinus. Much of the bone was roughened. A large sequestrum was present in the outer posterior part of the frontal sinus.

Recovery was uneventful.

CASE 13.—C. T., a Negro boy 14 years of age, gave a history of having had frontal headaches and tenderness of the entire right frontal region, with much discharge from the nose and throat, three years previously. There had been considerable pain and tenderness of the frontal region for the last few weeks.

Examination revealed diffuse swelling and tenderness over and around the right eye. The eye was completely closed. There was a moderate amount of pus in both sides of the nose, especially on the right. Roentgenograms showed increased density of all sinuses.

External drainage of the ethmoid cells and the frontal sinus was instituted. There was much pus in the frontal sinus. Swelling of the orbit and the frontal region continued; six days later an incision was made in the orbit, and about 2 drachms (7 cc.) of pus was evacuated. Through this opening roughened bone could be felt on the roof of the orbit and the anterior wall of the frontal region. Drainage tubes were inserted, and the patient did satisfactorily, but pus continued to come from the region of the frontal sinus and three weeks later the sinus was again opened. There was a large opening in the bone of the anterior wall of the right frontal sinus, and the cavity of the sinus was filled with granular and polypoid mucous membrane. The opening in the anterior wall was enlarged, all diseased bone being removed. This operative procedure was carried out through a horizontal incision over the cavity of the sinus. The cavity was packed with iodoform gauze. The wound healed rapidly, and a complete external ethmofrontal operation was done after all inflammatory signs had disappeared, with an uneventful recovery.

CASE 14.—L. A., a Negro boy 14 years of age, gave a history of pain in the right eye three weeks previously, swelling of the right eye and the right side of the forehead for the last five days and closure of the eye for the last two days. The patient had had a slight cold for one month, but there was no discharge from the nose or throat. The symptoms were so severe that a physician was called twenty-four hours previously, at which time the forehead was incised.

Examination revealed swelling of the right frontal region just to the right of the midline and extending to the hair line. This region had the appearance of having been incised, and from it pus was exuding. There were swelling of the right eye and pronounced tenderness over the entire forehead. The patient was taken to the operating room the same day, but little was done to the frontal region. He became stuporous within the next day or two; at that time Dr. Francis Murphey, of the neurosurgical division, performed a right frontal craniotomy, with drainage of an abscess of the right frontal lobe. There was extensive osteomyelitis of the frontal bone.

The patient rapidly grew worse and died.

CASE 15.—I. C., a Negro youth aged 17, gave a history of soreness of the frontal region. One year previously he had been struck on the forehead while playing football.

Examination revealed a small soft swelling in the midline of the frontal region and pus in the right middle meatus. A roentgenogram showed the frontal sinuses to be extremely large. All the sinuses were increased in density. Slightly to the

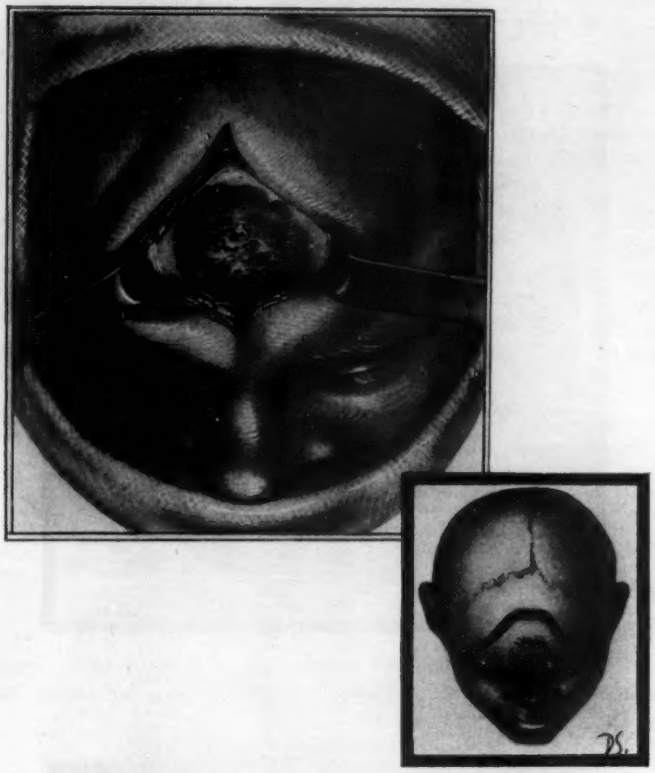

Fig. 11 (case 15).—Drawing of operative field, showing osteomyelitis of the frontal bone.

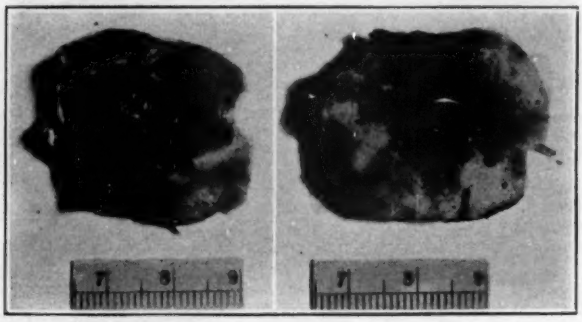

Fig. 12 (case 15).—Photographs showing the anterior and posterior surfaces of osteomyelitic bone after removal.

right of the midline, apparently in the anterior wall of the frontal sinus, there was an area of rarefaction, irregular in shape and about 2 cm. in diameter. A diagnosis of osteomyelitis of the skull was made.

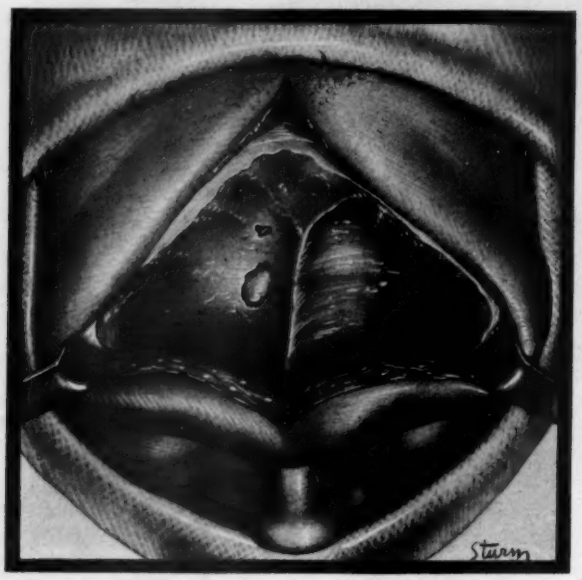

Fig. 13 (case 15).—Drawing of operative field, showing both frontal sinuses after exenteration and the dura exposed through the posterior wall of the frontal sinuses.

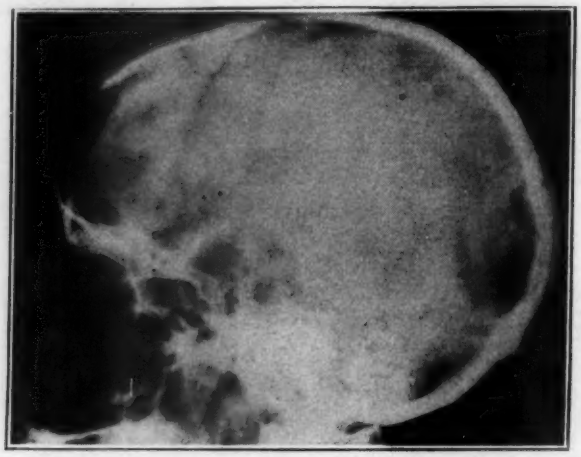

Fig. 14 (case 15).—Roentgenogram, showing formation of new bone.

With the use of local anesthesia, the following operative procedure was carried out. A midline incision was made through the soft tissues to the bone, and the periosteum was retracted laterally. The latter was free from the bone over an area

1½ inches (3.8 cm.) in diameter over the median portions of both frontal sinuses, beginning about ¾ inch (1.9 cm.) above the brow. The center of this area was slightly to the right of the midline. The bone was dark, and there were five moderate-sized openings into the frontal sinuses, through which pus and granulations were protruding. Much more of the bone was rough and worm eaten. The entire area was about 1 to 1½ inches (2.5 to 3.8 cm.) in diameter and was practically round. The periosteum was elevated slightly more widely, and an opening was made into the frontal sinuses above the necrotic area; this necrotic area was removed intact, with a fair amount of normal bone. A moderate amount of bone from the entire periphery of the necrotic area was removed with rongeurs. The frontal sinuses were extremely large and the mucous membrane was entirely polypoid. The frontal sinuses were both packed with iodoform gauze. No attempt was made to exenterate any mucous membrane, and no opening was made through the floor of the frontal sinuses into the nose. The patient made satisfactory progress, and nine days later a bilateral ethmosphenofrontal operation was done. As the mucous membrane of the posterior wall of the frontal sinus on the right side was removed,

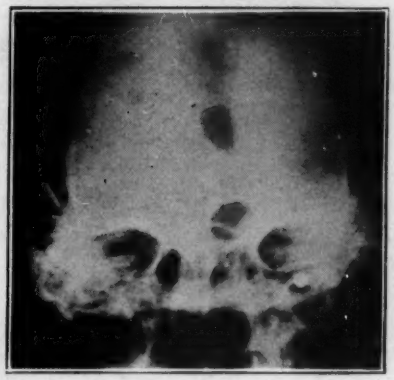

Fig. 15 (case 16).—Roentgenogram, showing peculiar round area of osteomyelitis in the frontal region.

there were two dural exposures, one about 0.5 cm. and the other about 1.5 cm. in diameter, both being located to the right of the midline, with the larger directly below the smaller. After the entire operation was completed the area of the frontal sinuses was packed with iodoform gauze and left wide open.

Recovery was uneventful.

CASE 16.—J. P., a Negro aged 30, gave a history of tenderness of the forehead for six months, swelling in this region for two weeks and frequent headaches and numbness of the entire scalp.

Roentgenographic examination revealed an area of rarefaction in the left frontal region of the skull which seemed to involve the entire thickness of the bone, and about 1 inch above this a similar area of rarefaction, 2 by 3 cm., extended down to the inner table.

Dr. Nicholas Gotten, of the neurosurgical division, carried out the following operative procedures: A T-shaped incision was made in the midline about 1 inch (2.5 cm.) above the supraorbital ridge. A fluctuating mass, filled with a thick grayish pus, was encountered, and on its removal an area of complete erosion of

the skull ½ inch (1.3 cm.) in diameter was observed. The surrounding bone was very soft and was removed over an area of about 1½ to 2½ inches (3.8 to 6.5 cm.), extending from the supraorbital ridge superiorly to the region of the coronal suture. Between the dura and the diseased bone there was a large mass of granulation tissue, which was removed. The left frontal sinus was filled with yellow

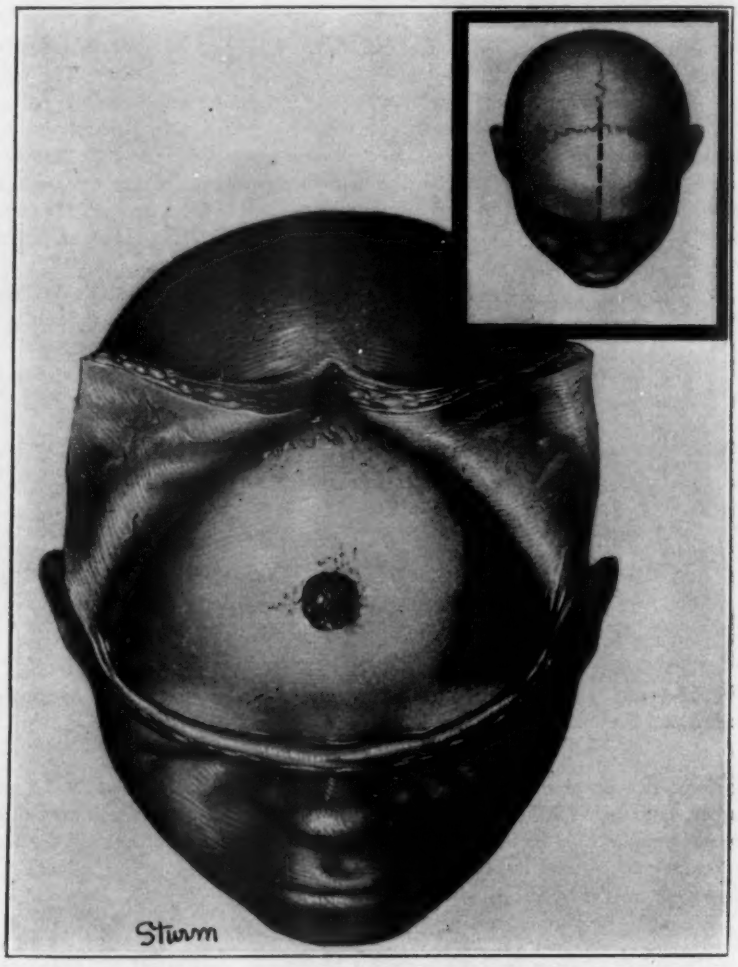

Fig. 16 (case 16).—Drawing of operative field, showing round opening in the osteomyelitic frontal bone.

purulent material and thickened membrane, which was exenterated. The wound was closed entirely externally, with one large drainage tube extending from the region of the frontal lobe through the left frontal sinus and the left ethmoid region into the anterior naris. The postoperative recovery of the patient was uneventful.

CASE 17.—R. McG., a boy 14 years of age, gave a history of having had a blow on the forehead one year previously. A few days later there were swelling and soreness of the forehead with a high temperature. The patient became delirious and

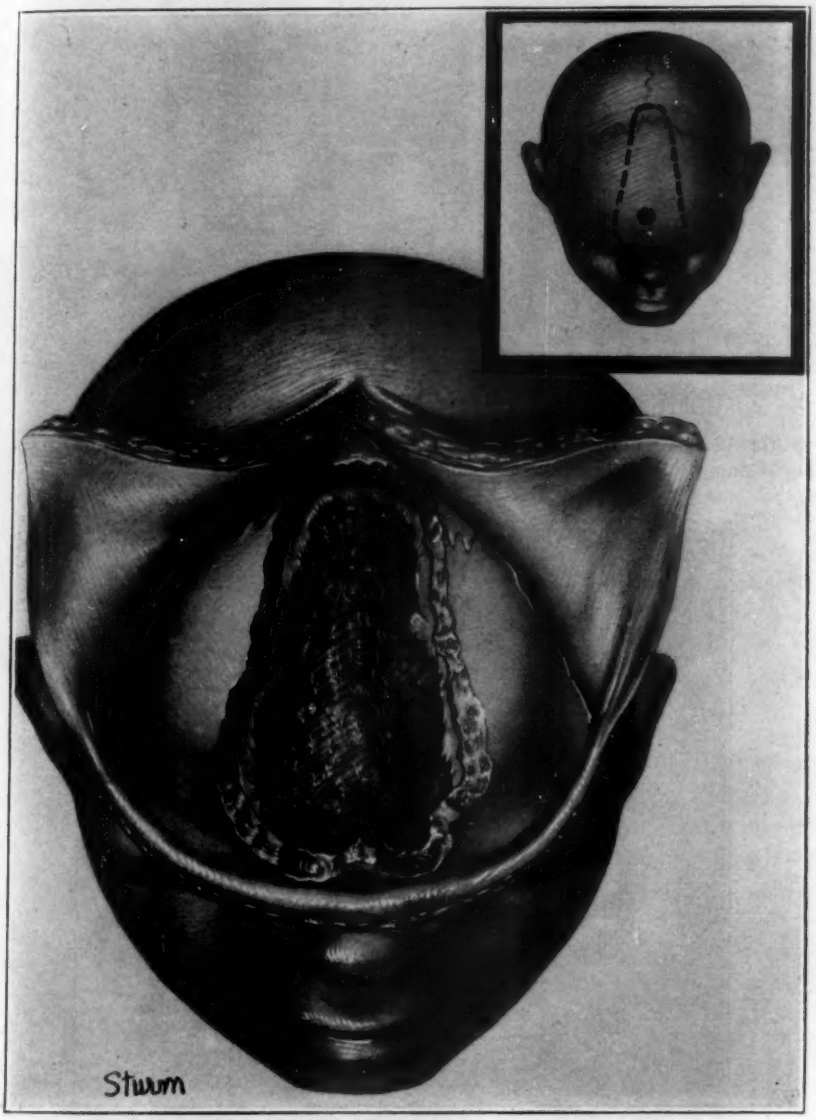

Fig. 17 (case 16).—Drawing of operative field, showing extensive involvement of the dura in the frontal region.

was brought to the hospital. Dr. Francis Murphey, of the neurosurgical division, drained subperiosteal and extradural abscesses through a midline incision into the frontal sinus. The patient went home and returned to the hospital eight months later, at which time a roentgenogram showed osteomyelitis of the skull.

With local anesthesia, Dr. Murphey made a midline incision in the frontal region, uncovering a large sequestrum, which consisted of a portion of the anterior and posterior walls of both frontal sinuses and a large portion of the septum. The

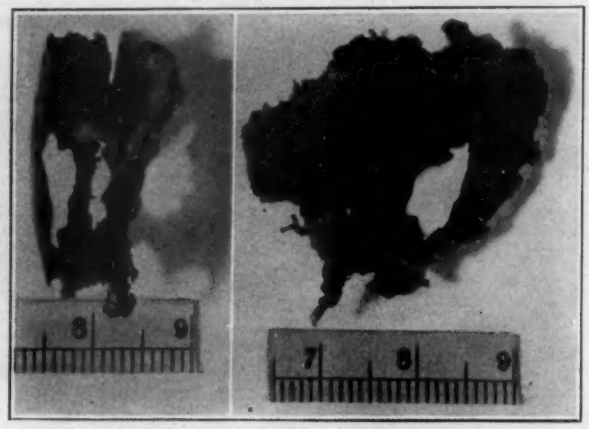

Fig. 18 (case 17).—Photograph of sequestrum from both frontal sinuses, showing septum between the sinuses and the anterior and posterior walls.

Fig. 19 (case 17).—Roentgenogram of reformed frontal sinuses three years after operation.

frontal sinuses were fairly well cleaned out, but no attempt was made at complete exenteration of these sinuses or of the supraorbital ethmoid cells, which were large and badly diseased.

Recovery was uneventful.

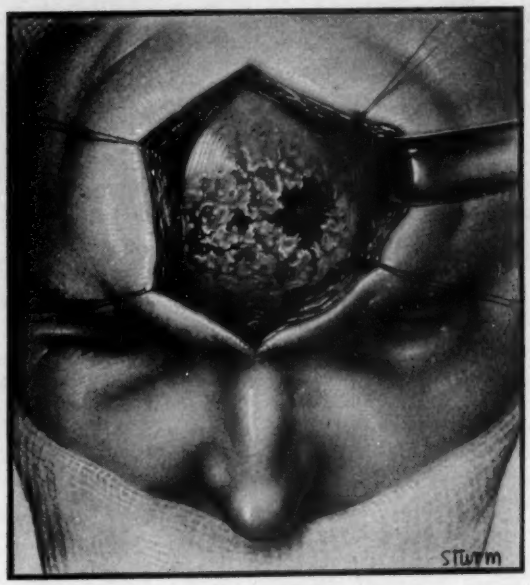

Fig. 20 (case 18).—Drawing of operative field in the frontal region.

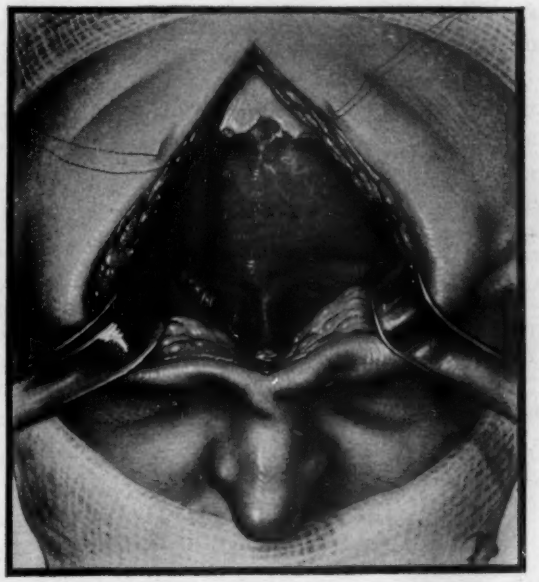

Fig. 21 (case 18).—Drawing of operative field, with exenteration of the frontal sinuses.

Within the last few weeks roentgenograms have again been taken. The interesting observation at this time is the formation of new frontal sinuses on both sides. As seen in the roentgenograms, the present frontal sinuses are as large and as regularly formed as the normal ones.

CASE 18.—Mr. J. N. was seen with a history of "sinus trouble" for many years, severe symptoms for the past ten months and severe pain in and swelling of the left frontal region for the past three weeks. External drainage of the left frontal sinus had been instituted three weeks previously in another city.

Examination revealed pronounced swelling of the left frontal region, with a fistulous tract into the left frontal sinus. A roentgenogram showed areas of osteomyelitis in the frontal region and advanced pansinusitis bilaterally.

A midline incision was made in the frontal region. The periosteum was absent from the major portion of the frontal region and the bridge of the nose, including the upper part of the nasal bones and the major portion of the floor of each frontal sinus and the supraorbital ethmoid cells. There were a large ragged opening of the anterior wall of the left frontal and several small openings of the anterior wall of the right frontal sinus, especially the lower part of the area which had no periosteum. The entire wall of both frontal sinuses and the floor of the right frontal sinus, as well as the remnant of the floor of the left sinus, were removed. Each frontal sinus, which was filled with a granular mass and pus, was cleared out. The dura was not uncovered. The wounds were packed with iodoform gauze.

About thirty hours after the operation the patient became delirious and died in twenty-four hours of general meningitis.

Among 18 patients there were 3 deaths (patients 8, 14 and 18). Patients 8 and 14 were boys 14 years of age, and patient 18 was a man 35 years old. They all had diffuse spreading osteomyelitis resulting from infection in the frontal sinus.

Patients 14 and 18 had been sick for a long period and lived only a short time after reaching the hospital. Patient 14 had a large abscess of the frontal lobe with meningitis, while patient 18 had diffuse purulent meningitis. Patient 8 was in the hospital several weeks and was probably treated too conservatively. A brain abscess was not recognized until late and was probably not present when he came into the hospital.

Thorough removal of the primary focus of infection and wide removal of osteomyelitic bone are the best means of preventing complications, such as meningitis and abscess of the brain.

512 Physicians' and Surgeons' Building.

LOCAL USE OF SULFATHIAZOLE IN OTOLARYNGOLOGIC PRACTICE

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Literature respecting the local use of sulfonamide compounds has of late been greatly increased by contributions from various battle fronts, and there seems to be no question that vast changes in emergency surgical technic have already occurred because of the employment of these valuable chemical agents. It is not proposed to review these interesting reports, far less to discuss the various theories advanced by immunologists and biochemists as to the exact fashion in which bacterial invasion is delayed or arrested. Perhaps a brief summary of personal experiences with the local use of one such agent—sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole)—may arouse comment and form part of the symposium on therapy with the sulfonamide compounds, which includes papers presented before the Eastern Section of this society by Marcotte and before the Middle Section by Furstenberg.

Sulfathiazole seemed to me preferable for local use because of its relatively slow solubility in tissue fluids; hence its action would seem to remain concentrated at the area of administration for somewhat longer periods, and the drug would thus pass less rapidly into the general circulation. It was felt, also, that while specific differences for inhibition of growth of bacteria might be established in vitro for different sulfonamide compounds, clinically sulfathiazole was equal to the task of holding almost any organism in check. While certain germs do not seem to be sensitive to ordinary blood levels of orally administered sulfonamide compounds, they are clinically much more vulnerable to the high concentrations obtained by local use. Certainly, the place in which to attack the metabolism of bacterial growth, dependent in all probability on the presence of paraaminobenzoic acid, is in the locality where that growth occurs. Establishment of the extent to which sulfonamide compounds act through blocking the utilization of this amino acid by bacteria is a problem for immunologists and biochemists, rather than for clinicians.

My associates and I have used sulfathiazole locally ever since it became readily available. Applied to mucous surfaces as a powder, it does not stop ciliary action; it disappears slowly, and its absorption seems much

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delayed. We used the highly alkaline 5 per cent solution of sodium sulfathiazole (p_H 10 to 11) only long enough to decide that its action was too disagreeable for comfort, and we were not surprised to learn of certain annoying after-effects. Various types of ointments, usually containing the drug in 5 per cent concentration, have been used by ophthalmologists, but although these have been helpful in cases of staphylococcic blepharitis, they have not in our experience been of any value in treatment of the so-called shipyard, or properly virus, keratoconjunctivitis which has appeared in recurrent epidemics along the Pacific coast during the past eighteen months, nor has the occasionally associated acute rhinitis due to irritating tears been helped by intranasal use of sulfathiazole as a powder or as an ointment.

Acute rhinitis, pharyngitis and laryngitis due to infection with the streptococcus and the hemolytic streptococcus yield quickly to the use of finely powdered sulfathiazole, blown into the nostrils, pharynx and larynx in small quantities by a powder blower, which can be turned in any direction. Gargling with a solution containing a 7.7 grain (0.5 Gm.) tablet of sulfathiazole in a quarter-cup of hot water will often bring much relief from local swelling and discomfort. The extreme redness and occasional dangerous edema of the throat, with severe pain in swallowing, associated with such conditions are usually greatly helped after one or two applications of the powder. If the temperature is also high, internal administration of the drug may be required, 7.7 grains being given every four hours day and night for twenty-four to forty-eight hours, with careful attention to the blood count and the hemoglobin level. Should pulmonary complications (severe bronchitis or pneumonia) supervene while the infection of the throat and trachea is yielding to local use of sulfathiazole, we have no hesitation in ordering the administration of sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) in full doses by mouth.

Sulfathiazole has not been found to have any apparent local or general effect on the ulcerations of Vincent's angina or on the painful fungations of tuberculosis or carcinoma of the larynx.

A limited number, perhaps 10 per cent, of patients with subacute suppuration of the maxillary sinus, accompanied by pain in the forehead and foul odor, have been helped to early recovery by injection of a few cubic centimeters of a 2.5 to 5 per cent suspension of powdered sulfathiazole crystals in physiologic solution of sodium chloride, after thorough irrigation of the sinus with warm saline solution. Untoward effects, however, followed in 1 case, in which the crystals had lodged as insoluble irritants in the edematous mucous membrane. Later, after radical removal of this membrane, its tough, gritty nature puzzled the pathologist, who described it as follows: "Representative pieces showed a vast accumulation of generally compactly arranged cells, many of

which could not be clearly identified as to type. However, the presence of occasional granulocytic leukocytes and the absence of blood vessels or other tissue, together with the clearly evident and numerous granulocytes and the mucus over the surface, most nearly fitted the picture of inspissated exudate. There were also many crystals, or clear spaces left by them, in the intercellular spaces. These crystals were rather long and spindle-like and were not of the cholesterol type. The history of the use of sulfathiazole makes it probable that it was this drug which was found in crystalline form. A malignant growth was suspected, but the sections proved the diagnosis of inspissated inflammatory exudate." The patient has since become decidedly allergic to the insufflation of sulfathiazole powder from a powder blower.

Another patient, of sedentary occupation, who had been taught many years ago how to wash out his own antrum through a large nasal window, had responded so quickly during an acute attack to treatment with the suspension of sulfathiazole in saline solution that he formed the habit of using the drug for several months thereafter. His nasal vestibule became irritated, and he became sensitive to drafts and picked up colds readily. His hemoglobin level had dropped to 74 per cent. Discontinuance of the drug brought prompt cessation of these symptoms.

Such an irritative action is said to be obviated by use of the so-called microcrystal preparations, but in all the cases we have encountered in which such effects were seen a rather definite chemical allergy to the drug seemed to be present. This observation is confirmed by reports from pharmacists who have been handling the powdered crystalline drug a good deal; they state that certain persons apparently become sensitized after long exposure, with the development of dermatitis of the hands, blepharitis and acute rhinitis.

Combinations of sulfathiazole with weak shrinking agents have seemed beneficial for instillation with a dropper, with the head thrown back. Among these, we have recently been experimenting with a solution, mildly alkaline (p_H 9), which contains sodium sulfathiazole sesquihydrate and 1 per cent *dl*-desoxyephedrine hydrochloride, with 2 per cent anhydrous sodium sulfite as a preservative.[1] As with many similar preparations, the shrinking effect of the synthetic ephedrine component produces local relief and allows the sulfathiazole to penetrate deeply under the turbinates. This preparation is also effective in treatment of subacute dacryocystitis, often permitting through and through lavage without the necessity of probing, with shortening of the duration of treatment. The solution is also valuable for washing out the salivary ducts when secondary infection has occurred during attempted passage of small calculi. Suspensions of sulfathiazole might under similar con-

1. This preparation was supplied for experimental use by E. R. Squibb & Sons, New York.

ditions cause further obstruction. The solution employed, and other alkaline preparations of sulfathiazole, are precipitated by solutions of cocaine.

Another experimental preparation which remains in the antrum for some time and seems to allay subacute suppuration rather quickly is a chondrus, water-soluble jelly containing 5 per cent sulfathiazole;[2] this substance can readily be injected through the Lichtwitz needle after lavage of the antrum.

An excellent suspension of 5 per cent microcrystalline sulfathiazole in 1 per cent aqueous solution of paredrine hydrobromide[3] is now commercially available. But while quick relief of nasal obstruction occurs, and the powder is carried well into the nose by postural application, the usual secondary swelling that follows the use of ephedrine and its substitutes shortly reproduces the initial discomfort and is likely to lead to excessive use of the preparation, with less effect on each subsequent occasion.

None of these combinations is free from the possibility that allergic responses may be excited in susceptible persons, and it does not seem possible to determine in advance whether such sensitivity exists.

Wounds of the face, particularly those involving compound fractures of the nose, cheek or frontal sinus, respond extremely well to the local use of sulfathiazole powder. Such wounds should be carefully cleansed and dried and then dusted thoroughly and deeply with the powder, after hemostasis and before any attempt at suture is made. Fractures of the jaw and tooth sockets in which much of the jaw is exposed after dental extractions react most favorably to the local use of this drug.

After the external frontal or the transorbital ethmoid operation, after entrance to the maxillary sinus or the ethmoid cells by way of the canine fossa, after the intranasal approach to the ethmoid cells or the sphenoid sinus and after tonsillectomy, insufflation of a thin coating of sulfathiazole powder seems to keep down pain and offensive saprophytic odor to a remarkable degree. Similarly, edema and discomfort after laryngofissure and tracheotomy are much reduced, and in all these procedures healing is speeded up. A sterile powder blower is available at all times in our operating and dressing rooms.

In almost every case during the past eighteen months, we have found it possible after mastoidectomy to make primary closure of the wound by means of careful hemostasis and dusting in of sufficient sulfathiazole pow-

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2. This preparation was sent out for trial by Abbott Laboratories, North Chicago, Ill.

3. The solution employed is paredrine hydrobromide aqueous, which contains p-hydroxy-α-methylphenethylamine hydrobromide, 1 per cent, made isotonic with sodium chloride and preserved with merthiolate, 1:100,000, and is marketed by Smith, Kline & French Laboratories, Philadelphia.

der to cover the walls of the operative cavity. It is undesirable to fill the cavity, for an excess of the powder may act as a foreign body in a large granulating wound. Gauze packs or rubber drains are not used.

Acute suppuration of the middle ear is not suitable for local treatment with sulfathiazole. In cases of the chronic form, with a wide perforation, it is often possible, however, to remove debris from the attic with the middle ear cannula, dry the cavity carefully and then blow in a minute portion of the powder. This will often prevent odor and drainage for a month or more. As with boric acid, however, one must avoid plugging the opening, since such a powder "sets" like cement into a cake, which is both dangerous and hard to dislodge.

Thus far we have seen no evidence of renal disturbance from the local use of sulfathiazole. Accordingly, one may conclude that this agent is a safe and valuable adjunct to the local management of infected wounds and in the local treatment of acute nasopharyngitis, laryngitis and tracheitis. Its employment in cases of acute sinusitis and convalescence therefrom seems occasionally valuable. Sensitivity to its local use invites attention from the pharmacologist, as well as the immunologist and the specialist in allergy; this is a rare but annoying complication, which may appear more frequently as the public makes uncontrolled use of sulfathiazole in tablet or powder form for various purposes.

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LOCAL USE OF SULFATHIAZOLE POWDER FOR ACUTE PHARYNGEAL INFECTIONS

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A study of acute pharyngeal infections treated by the topical application of sulfathiazole powder in the otolaryngologic dispensary of St. Luke's Hospital is presented here. Sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) is the thiazole analogue of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) and was first reported on by Fosbinder and Walker [1] and by Lott and Bergeim.[2] These authors described the methods of preparation and their experiments with these drugs against streptococcic and pneumococcic infections in mice. The original work on the physical and chemical characteristics of sulfathiazole and its salt was done at that time, and tests for the estimation of the drug in the body were described.

Van Dyke and his co-workers [3] showed the rapid metabolism of this drug in the body. Sulfathiazole was proved to be more rapidly absorbed than other sulfanilamide derivatives, the concentration in the blood reaching its highest level in one to three hours after ingestion of the drug. Moreover, it disappeared and was excreted more rapidly. These results led to the conclusion that this drug must be less toxic than the others.[4] It may be applied to the same types of infection and bacteria as the other derivatives and has been shown by many authors to be superior to sulfanilamide in most cases.[5]

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1. Fosbinder, R. J., and Walter, L. A.: Sulfanilamide Derivatives of Heterocyclic Amines, J. Am. Chem. Soc. **61**:2032 (Aug.) 1939.

2. Lott, W. A., and Bergeim, F. H.: 2-(*p*-Aminobenzenesulfonamido)-Thiazole: A New Chemotherapeutic Agent, J. Am. Chem. Soc. **61**:3593 (Dec.) 1939.

3. Van Dyke, H. B.; Greep, R. O.; Rake, G., and McKee, C. M.: Observations on the Toxicology of Sulfathiazole and Sulfapyridine, Proc. Soc. Exper. Biol. & Med. **42**:410 (Nov.) 1939.

4. Long, P. H.; Haviland, J. W., and Edwards, L. B.: Acute Toxicity, Absorption, and Excretion of Sulfathiazole and Certain of Its Derivatives, Proc. Soc. Exper. Biol. & Med. **43**:328 (Feb.) 1940.

5. (*a*) McKee, C. M.; Rake G.; Greep, R. O., and Van Dyke, H. B.: Therapeutic Effects of Sulfathiazole and Sulfapyridine, Proc. Soc. Exper. Biol. & Med. **42**:417 (Nov.) 1939. (*b*) Cooper, F. B.; Gross, P., and Lewis, M.: Chemotherapeutic Evaluation of Sulfanilamide Derivatives of Heterocyclic Amines, ibid. **42**:421 (Nov.) 1939. (*c*) Rake, G., and McKee, C. M.: Action of Sulfathiazole and Sulfamethylthiazole on Staph. Aureus, ibid. **43**:561 (March) 1940. (*d*) Bliss, E. A., and Ott, E.: Effects of Sulfapyridine, Sulfathiazole, and Sulfametylthiazole upon Severe Staphylococcus Infections in Mice, ibid. **43**:706 (Feb.) 1940.

The favorable results obtained with this drug given by mouth and applied locally for acute general surgical infections have been widely reported in the current literature. In the field of otolaryngology, however, reports of its use locally are not so numerous. Ayuyao, Yambao and Simuangco,[6] in a comparative report of several solutions used for antral irrigations in cases of chronic disease of the maxillary sinus, including physiologic solution of sodium chloride, potassium permanganate and collargol, stated that the highest percentage of recoveries followed the use of a solution of azosulfamide after irrigation with a saline solution. They did not mention any experiments with sulfathiazole. Livingston[7] noted shortening of the postoperative period and greater incidence of primary healing when crystals of sulfanilamide or sulfathiazole were locally implanted after simple mastoidectomy. Turnbull[8] claimed excellent results in the treatment of chronic sinusitis with an intranasal spray of 5 per cent sodium sulfathiazole solution. The experiences of my associates and me with application of the drug in antrums following the Caldwell-Luc procedure have not been encouragnig. To date, however, no reports of the use of sulfathiazole locally on the pharyngeal mucosa have been available.

METHOD

After the histories of the patients in this series had been obtained and physical examinations and routine cultures of material from their throats had been made, sulfathiazole powder was applied to the pharyngeal mucosa with a compressed air powder syringe. The powder was applied until it thickly caked the involved areas. Nasopharyngeal applications were made through the nose or with a shortened eustachian tube catheter placed behind the soft palate. The dose, which was difficult to ascertain, varied between 1 and 2 Gm. per treatment. Much of this was lost by expectoration, but examination at one, two, three and four hour intervals following treatment revealed a surprisingly large amount of the relatively insoluble powder clinging to the nasopharyngeal and pharyngeal mucosa, in the vallecula and in the crypts of the tonsils. The patients were instructed to avoid eating or drinking for two hours following treatment and were told to use no other form of therapy. They were seen after twenty-four hours, at which time they were questioned as to when relief was first noted and then reexamined. In

6. Ayuyao, C. D.; Yambao, C. V., and Simuangco, P.: A Comparative Study of Some Treatments of Inflammation of the Maxillary Antrum, J. Philippine M. A. **20**:451 (Aug.) 1940.

7. Livingston, G. S.: Local Sulfonamide Therapy in Acute Mastoiditis, J. A. M. A. **117**:1081 (Sept. 27) 1941.

8. Turnbull, F. M.: Chronic Sinusitis, J. A. M. A. **116**:1899 (April 26) 1941.

some cases specimens from which to determine the level of free sulfathiazole in the blood were obtained. The patients were subsequently seen at twenty-four hour intervals until the termination of the disease.

MATERIAL

The patients used in this study were for the most part members of the hospital house staff and nursing personnel. Patients from the outpatient department were also included. The criteria for inclusion in the series were: (1) a history of sore throat or dysphagia with or without systemic manifestations and (2) physical findings consistent with the diagnosis of acute infection of the pharynx or nasopharynx. Patients with an adequate history without objective evidence, or vice versa, were discarded.

TABLE 1.—*Types of Disease Represented*

Disease	Number of Cases
Acute follicular tonsillitis	9
Acute pharyngitis (mild)	7
Acute pharyngitis (severe)	7
Acute pharyngitis with coryza (severe)	4
Acute nasopharyngitis	5
Vincent's ulceration of tonsil	2
	34

The series consists of 34 cases of acute infection of the pharynx or nasopharynx. Twenty-four of the patients were female. The ages of the entire group ranged from 10 to 60 years, with an average of 28 years. The distribution as regards type of disease is indicated in table 1.

BACTERIOLOGY

Table 2 represents the organisms found in the cultures of material from the throats of patients in the series and in routine cultures of material from the throats of student nurses entering during 1941-1942, in approximately the same period as that in which the present study was being carried out. The throats of the nurses were objectively normal.

Table 3 shows the incidence of the organisms found in the cultures taken from patients with the different types of disease. These tables show that the chief offenders are Streptococcus viridans, Staphylococcus aureus, Staphylococcus albus, beta streptococci and a mixed culture of beta streptococci and Staph. aureus. A remarkable parallelism is seen in the distribution of organisms from diseased and normal throats. These organisms are all well enough known pathogens and also occur in normal throats. This suggests attenuation of the virulence of the

TABLE 2.—*Organisms Isolated*

Organism	Number of Cultures	
	Patients	Nurses
Str. viridans	8	8
Staph. aureus	4	9
Str. beta	4	4
Staph. albus	3	4
Staph. aureus Str. beta	7	2
Staph. albus Str. beta	2	1
Str. viridans Str. beta	1	2
Str. viridans Staph. aureus	1	..
Str. viridans Str. beta Staph. albus	1	..
Str. beta Friedländer's bacillus	1	..
	32	30

TABLE 3.—*Incidence of Organisms in Different Types of Disease*

	Acute Tonsillitis	Severe Acute Pharyngitis	Mild Acute Pharyngitis	Acute Pharyngitis with Coryza	Acute Nasopharyngitis
Str. beta	3	1	..	..	..
Str. beta Staph. albus	2	..	..	..	..
Str. viridans	1	2	2	..	3
Staph. aureus Str. beta	1	2	2	..	2
Str. beta Friedländer's bacillus	1	..	..	..	..
Staph. aureus	1	..	2	1	..
Staph. albus	..	1	1	1	..
Str. viridans Str. beta Staph. albus	..	1	..	..	..
Str. viridans Str. beta	..	..	..	1	..
Str. viridans Staph. aureus	..	..	..	1	..

organisms. Topley and Wilson,[9] however, called attention to the low virulence and pathogenicity of Str. viridans and its frequent occurrence in normal throats; so it must be assumed that other organisms varying in strain must also alter their virulence from time to time. It is significant, however, that beta streptococci were found most frequently in pure culture in acute follicular tonsillitis.

RESULTS OF THERAPY

The inherent error of the statistical method in application to a small series is recognized. However, it is the most readily available means of indicating the trend of a new mode of therapy.

In the entire group of cases the duration of the presenting complaint, which in every instance was that of "sore throat," varied between four and ninety-six hours, with an average of forty and two-tenths hours. Only 9 (29 per cent) of the patients had any systemic manifestations.

TABLE 4.—*Duration of Disease and Interval Before Improvement*

Condition	Subjective Improvement, Hours	Objective Improvement, Hours	Duration, Days
Acute follicular tonsillitis	8.7	24.0	2.5
Acute pharyngitis (severe)	12.0	25.7	2.2
Acute pharyngitis (mild)	8.2	30.0	2.6
Acute nasopharyngitis	5.8	26.4	1.8

Subjective improvement was noted in one to twenty-four hours after the first treatment, with an average of ten hours. It is suggested that the latter figure may be high because certain of the patients could not remember the exact time of relief. These were indicated as having relief within twenty-four hours. Objective improvement in the entire series was obtained in from twenty-four to fifty-six hours, with an average of twenty-four and six-tenths hours. From one to four treatments at twenty-four hour intervals were required, with an average of two and two-tenths treatments. The duration of the disease after treatment was instituted varied between one and three days, with an average of two and four-tenths days. Of 18 of these patients who were followed at twenty-four hour intervals with determinations of the free sulfathiazole in the blood, only 5 (27.7 per cent) showed any presence of the drug, the levels varying between 0.4 and 0.9 mg. per hundred cubic centimeters of blood.

Table 4 shows in hours the average interval for subjective and objective improvement in each of the various conditions and the average duration of the disease in days after treatment had been begun. These

9. Topley, W. W. C., and Wilson, G. S.: The Principles of Bacteriology and Immunity, ed. 2, Baltimore, William Wood & Company, 1937.

findings indicate that subjective and objective improvements with this method of treatment are relatively rapid, especially in cases of acute nasopharyngitis. Furthermore, the duration of the disease is decreased considerably.

It must be noted that in 1 case of follicular tonsillitis (in which the culture showed beta streptococci and Friedländer's bacillus) the patient, who had received treatment, returned three days later with an incipient peritonsillar abscess, which was promptly aborted by sulfanilamide given orally and hot irrigations of the throat. Furthermore, 3 patients with acute pharyngitis with coryza obtained subjective relief from their pharyngeal symptoms within an average time of three hours, but the disease subsequently went on to run the course of a typical catarrhal rhinosinusitis. Although these 3 patients had no recurrence of their pharyngeal symptoms, no objective improvement of the pharynx was noted until resolution of the sinusitis began. In 2 cases of ulceration of the tonsil due to Vincent's organisms no subjective or objective improvement was obtained from this therapy.

Kernan,[10] Rhoads and Afremow,[11] Richards [12] and Hughes [13] have all questioned the oral use of sulfonamide compounds in acute uncomplicated diseases of the pharynx. Rhoads and Afremow [11] stated that sulfanilamide effected no change in the course of acute tonsillitis as regards severity of symptoms or period of incapacity. There is some disagreement as to its effect on the incidence of complications. Rhoads and Afremow pointed out that in some instances the reactions from administration of the drug were severe enough to cause concern.

SUMMARY AND CONCLUSIONS

A hitherto undescribed method of treating acute infections of the pharynx and nasopharynx is presented.

The method rapidly produces subjective and objective relief and materially shortens the course of the disease.

The possibility of systemic damage from the use of sulfathiazole is negligible with this method of treatment.

The method is inexpensive and is easily carried out on ambulatory patients.

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10. Kernan, J. D.: Infections of the Mouth, Pharynx, and Respiratory Tract, Bull. New York Acad. Med. **17**:674 (Sept.) 1941.

11. Rhoads, P. S., and Afremow, M. I.: Sulfanilamide in the Treatment of Sore Throat Due to Hemolytic Streptococci, with Controls, J. A. M. A. **114**:942 (March 16) 1940.

12. Richards, L. G.: Treatment of Diseases of the Throat, J. A. M. A. **115**: 501 (Aug. 17) 1940.

13. Hughes, L. W.: Diseases of the Nasopharynx, Mississippi Doctor **18**:261 (Oct.) 1940.

ON PLANNING NASAL SURGERY

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The material which forms the background of this discourse is not new. However, an attempt is made to mold it into something approaching a useful pattern by which a given nasal operation may best be made to attain its ends.

To my mind the first desideratum in any treatment is ultimate and, if possible, permanent improvement. Immediate improvement should not be permitted to weigh against the end result.

Improvement in what? In function, first and last. Unless one is interested in a purely cosmetic reconstruction this is practically the only goal. The surgical fashion, whether it be of the moment or a relic of a previous era, is of no importance. The wetness or dryness or straightness or cleanness or pinkness of the airways may interest the doctor but not the patient. The patient's measure of a successful treatment—and it should be the physician's—is a nose that works, a nose of which he is not conscious. It is my contention that what will make a nose work often lies outside the routine of the standard operative procedures and demands individual planning for practically every case.

Before laying down such a plan one must stop for a moment to examine the nature of the functions which one is striving to restore and maintain. With these clearly in mind the logical treatment often suggests itself more or less automatically. These functions are two: smell and air conditioning. Under the latter heading come humidification, heating, filtration and self cleansing. I shall point out briefly the intimate bearing of these functions on surgical problems.

1. The sense of smell demands an intact nerve, a moist mucosa and an airway which is not only open but streamlined to carry air to the olfactory end organ. This involves the relationships of the septum and its irregularities, the turbinates and the shape and direction of that constricted point 1 cm. above the external naris which determines the nature and shape and direction of the air stream.

2. Humidification demands that the surfaces of the two nasal fossae be adequately exposed, adequately nourished and adequately stimulated

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to disgorge approximately 1,000 cc. of water in twenty-four hours. Not only is humidification necessary for the maintenance of health of the bronchial tree (the difficulties attendant on cannulation are well known) but it is the first essential to ciliary activity. Dry spots in the nose are never ciliated. Complete humidification requires a full quota of turbinated bodies and their glands.

3. Heating demands that the conchae be capable of radiating 70 large calories in twenty-four hours. Inadequately heated air creates and maintains irritations and infections of the respiratory tract. Heating requires wide surface exposure and blood supply unobstructed by scars and pressures. It also requires a full quota of turbinal tissues.

4. Filtration, which includes the removal of particulate matter and micro-organisms, requires moist surfaces, free access to them and an air stream so directed as to utilize to greatest advantage the impingement effect.

5. Filtration entails the continual purging of the filter, a function seldom apprehended yet one without which the nose becomes a nuisance and a menace. The cleansing mechanism, consisting of an unbroken surface of ciliated epithelium covered by a tough mucous blanket, constitutes an efficient belt conveyer. The cilia have no part in filtering the air. They function solely in keeping the nose clean. In order to accomplish this effectively there must be no inactive areas, no dry spots. These are responsible for more chronic nasal trouble than any other single element, infected sinuses included; in fact, they are often the perpetuating factor in chronic sinusitis. It is common experience that pain and inflammation are characteristic of dry, overventilated membranes.

Having thus clearly in mind what is to be accomplished, one is now in a position to formulate the surgical plan. Scars must be made and areas denuded, and structures may have to be sacrificed. But some ways of doing this are better than others. Extensive scars occurring in eyes, ears and noses are more likely to prove incapacitating than scars elsewhere on the body surface and should therefore be made with more circumspection and with at least equal regard for location. It may make little difference so far as the gain in ventilation is concerned whether one removes a septal spur or cauterizes or removes a portion of a contiguous turbinate, but the direction and concentration of a new air stream thus set up may produce a headache or a tubal disturbance, and so the *plan* becomes important. How it may be executed is even more so. Two operators ostensibly employing the same methods may not attain the same results. Two artists working from the same palette on

similar canvasses turn out very different pictures of the same subject. This is because of differences not only in skill but also in interpretation and point of view.

Surgical therapy of the nose may be dealt with under five headings: (1) no intervention at all; (2) operation for ventilation (admitting air, redirecting air and relief of air pressures, positive and negative); (3) operation for relieving mechanical pressure; (4) operation for drainage (evacuating purulent and other secretions), and (5) operation for eradication of diseased tissue.

No surgical intervention at all is excellent treatment in those cases in which operation does not have a reasonable chance of accomplishing a very definite, predetermined result. The trial and error method (unless backed by experience vast enough to eliminate most of the error) is hard on the patient. This is not intended to embody the criticism which it seems to convey. One is often confronted by a chain of symptoms which have failed to respond to previous surgical treatment, and the temptation to remove another spur, open another sinus or excavate a nasofrontal duct is great and understandable. An additional operation is justifiable if the symptom in point is directly traceable to the defect. More operation is almost never an improvement on too much operation gone before. The most pathetic figures I have seen are the victims of multiple operations—a shockingly persistent miscomprehension of the surgical principles involved.

An operation for ventilation will often accomplish its purpose more effectively if it is so conducted as to do nothing but ventilate. While it is as yet undetermined whether air pressures which cause pain are positive or negative, or either, there are undoubtedly pains which can be relieved by merely making an opening into a sinus. If this is made large with the idea of keeping it open, one immediately makes fresh trouble and creates new causes of headache. The exposure of the sinus membrane to blasts of air may set off attacks of pain through direct irritation of the nerve endings or may so incapacitate the cilia through drying that stasis, low grade infection and finally metaplasia take place.

A similar condition may obtain in the nose itself. Pain and discharge may be due to overventilation or the concentration of an air stream on a restricted, sensitive area. If an operation designed to redistribute and redirect the stream succeeds in doing so it may cure the pain. If it fails in this respect, no matter what else it accomplishes, it will fail to relieve the pain. It is useful in such cases before operating to study the effect produced by obstructing one or the other side of the nose with cotton for several hours at a time. If this does not alleviate the headache a redistributing operation will have relatively little chance of success. If

a sphenoid opening is to be made for ventilation it is my practice to make it small, to prevent closing by punching the edges clean and to avoid the ostium, regarding it as a mechanism whose function can ill be spared.

If drainage is the chief object of the operation it can be best restored by conserving and fostering the rehabilitation of the ciliated epithelium and the glands which produce the mucous blanket. The surest way of destroying these is to establish a large opening in a location exposed to air currents. While this may seem momentarily preferable, it establishes a situation which eventuates in the destruction of the cilia and the inspissation of secretions which can no longer be spontaneously evacuated and which invite infection and further surgical intervention.

The effectiveness of "window" openings under the inferior turbinate into the maxillary sinus is due largely to the protected position of the opening, shielded as it is from direct air currents, and to the integrity of the ostium.

Before surgical eradication of diseased tissue is attempted it should be established that what will take the place of this tissue will be preferable to what is removed. Malignant growths and most tumors raise little doubt in this respect. They should come out cleanly whenever possible (neoplasms above the level of the floor of the nose are said to metastasize later than those below it). What should be done about them if they cannot be removed cleanly by surgical methods is another story and not part of this discussion.

Tissues requiring careful scrutiny are those chronically inflamed and infected, and especially allergy-ridden membranes. If the nature and the distribution of infection within the membrane are such that it impairs the health and comfort of the patient, then the infected tissue should be removed, ordinarily through a radical operation. In this situation the external approach in competent hands gives better promise of relief, because it reaches the involved tissues directly without sacrificing others essential to the physiologic activities of the nose.

Allergic membranes will presumably be replaced after removal with other allergic membranes, since allergy is an attribute of the person and not a local disorder. In my experience allergic tissues should be regarded surgically on the basis of their potentialities aside from allergy. They should be removed if they obstruct or if a concurrent infection demands it. Far from constituting a contraindication to surgical intervention, allergic symptoms in the nose and chest are often alleviated by a judicious reestablishment of something approaching physiologic airways. I am aware that sometimes operation has aggravated symptoms and has permitted fresh sensitization. Against this the patient should be guarded by choice of location and season.

SUMMARY

The logical end to which all treatment should be directed is ultimate improvement in function.

How this is to be accomplished should be definite in the mind of the operator at the start, so that he may not by inept surgical methods set up new disturbances.

The requirements in a given case are not always met by an unmodified standard procedure.

Nasal functions which must prevail in the end in order to establish a working nose are olfaction, adequate humidification and heating, filtration and the ability of the membrane to keep itself clean through an active and effective ciliary mechanism.

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RECOVERIES FROM STAPHYLOCOCCIC MENINGITIS FOLLOWING BACTERIOPHAGE THERAPY

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Before undertaking a more detailed consideration of our patients who suffered from staphylococcic infection of the meninges, we have presented a review of staphylococcic meningitis [1] as reported in the literature. We were able to find records of 48 acceptable examples of recovery from this disease, a number sufficiently small to indicate the malignant nature of this localization of staphylococcic infection. We plan to discuss now the patients with staphylococcic meningitis for whom we have been privileged to furnish bacteriophage service, including in this discussion not only those who had a recognized invasion of the blood stream, so as to belong in our series of 500 patients with staphylococcemia,[2] but also patients suffering from meningitis without adequate evidence of staphylococcemia and hence omitted from the series with sepsis. The patients included in this series with staphylococcemia will be designated by their appropriate serial numbers. In the present paper we purpose to present the records of 10 patients who recovered from meningitis and of 1 additional patient who apparently recovered from meningitis and was discharged from the hospital but succumbed later to an abscess of the brain. The case histories of some of these patients have already been recorded in the literature, and some of them will be found not wholly acceptable as examples of diffuse inflammation of the leptomeninges. Each of them, however, may teach a lesson in regard to the difficult problem of staphylococcic meningitis.

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1. MacNeal, W. J.; Frisbee, F. C., and Blevins, A.: Staphylococcic Meningitis from Hippocrates to Le Gendre and Beaussenat: A Mortal Disease, Arch. Otolaryng. **37**:199-208 (Feb.) 1943; Reported Recoveries from Staphylococcic Meningitis, 1893 to 1941, ibid. **37**:349-370 (March) 1943.

2. MacNeal, W. J.; Frisbee, F. C., and McRae, M. A.: Staphylococcemia, 1931 to 1940: Five Hundred Patients, Am. J. Clin. Path **12**:281-294 (June) 1942.

REPORT OF CASES

CASE 1.—*Girl, aged 7 years; comminuted occipital fracture; extrusion of brain substance; diffuse staphylococcic leptomeningitis; commercial bacteriophages given by intrathecal injection; ventriculography; recovery without sequelae.*

W. G., a girl aged 7 years, suffered fracture of the skull in an accident on March 5, 1933. Immediate examination at 12:55 p. m. on this date disclosed a comminuted fracture of the occiput with extrusion of brain substance and lacerated meninges. After removal of the lacerated tissue and surgical dressing, a roentgenologic examination revealed small fragments of bone remaining within the cranial cavity. The patient regained consciousness on the third day but remained very drowsy with temperature not above 101 F. until March 11.

On March 16 the child complained of pain beneath the wound and severe headache. The wound was probed, and considerable serous fluid was released. The

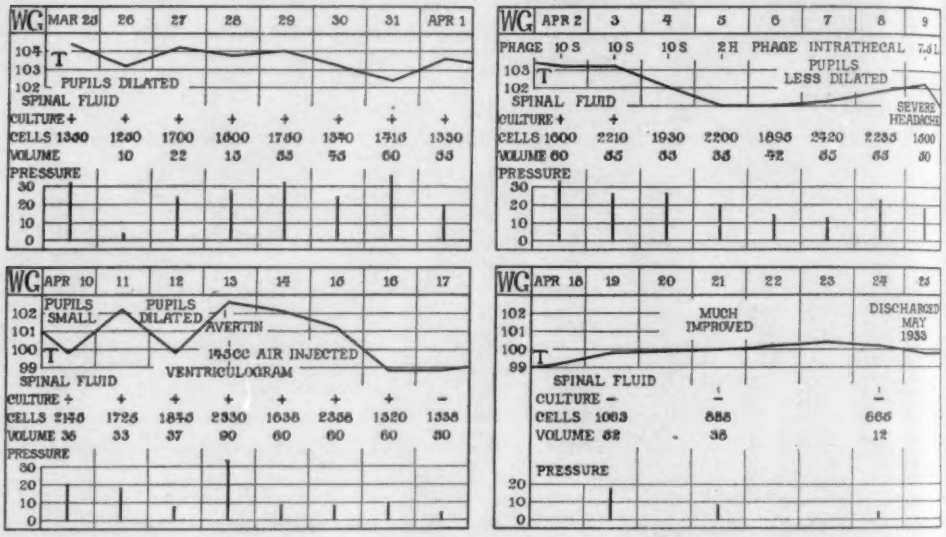
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Fig. 1.—Abbreviated clinical chart of W. G. *T*, temperature; *P*, pulse rate.

temperature reached 102.8 F. On the next day the temperature rose to 104 F., and there were pain, stiffness and tenderness in the back of the neck. The pupils were dilated and sluggish. The tissues were bulging through the craniotomy wound. Tetanus antitoxin was administered on this day. The septic temperature continued, ranging from 99 to 104.4 F. On March 20 a spinal tap yielded 10 cc. of turbid fluid under pressure of 32 mm. of mercury. The cell count was 1,600, of which 95 per cent were polymorphonuclears. The culture showed nonhemolytic Staphylococcus aureus. On March 25 fluid obtained by a second spinal puncture gave a cell count of 1,350. At this time the scalp wound was healed, but the scalp was somewhat edematous over the cranial defect. The patient was now seen by Dr. Foster Myers, of Toledo, Ohio, who has kindly furnished us the records of the case.

Some of the more important features of the clinical record are shown in figure 1. Daily spinal taps were done from March 25 to April 17, inclusive. The

cell count remained persistently above 1,000, and whenever a culture was attempted it always yielded a growth of staphylococci, until a negative result was obtained on the fluid of April 17. Meanwhile stock bacteriophage was supplied from New York in response to a request from Dr. Myers, but this was not used. On April 2 we received a specimen of the spinal fluid and were able to prepare a potent specific phage active against the staphylococcus present. This also was sent on to Toledo but was not used. On April 2 an intrathecal injection of 10 cc. of staphylococcus bacteriophage prepared by the Swan-Myers Company was administered and this dose was repeated on April 3 and April 4. On April 5 an intrathecal injection of 2 cc. of d'Herelle bacteriophage was given. During these days the temperature assumed a lower level. However, the tests of the bacteriophages carried out in the laboratory at Toledo were not encouraging. On April 9 an intrathecal injection of 7.5 cc. of staphylococcus bacteriophage prepared by Eli Lilly and Company was given. The severe headache at this time was thought to be related to the merthiolate in this preparation. No further bacteriophage was used, although the specific phage sent on from the Post-Graduate Laboratories in New York proved to be potent against the specific bacterial strain when tested in Toledo. On April 13, with the patient under anesthesia induced with avertin with amylene hydrate, an intrathecal injection of 145 cc. of air was administered and a ventriculogram was made, which revealed no evidence of meningeal adhesions except at the margins of the fracture; nor was there any other evidence of deformity or distortion in the brain. Subsequent to the making of the ventriculogram the temperature came down to normal on April 16, and the spinal fluid withdrawn on April 17, 19, 21 and 24 gave no growth in the cultures. On May 5 spinal tap yielded 15 cc. of fluid at a pressure of 8 mm. of mercury and with a cell count of 75. The patient was sitting up at this time.

In the laboratory tests carried out at Toledo it was impossible to obtain evidence of lysis of the cultures by any of the bacteriophages used in therapy. Until April 10 all the cultures of spinal fluid gave a diffuse growth in broth. However, beginning on April 10 the cultures made from the spinal fluids seemed to contain "increasing amounts of agglutinins and precipitins." There was a definite clumping of the bacteria in the cultures and marked precipitation. Spinal fluid obtained during this period, when added to subcultures of the organism obtained at an earlier date, caused these also to agglutinate and precipitate. When the specific phage prepared in New York was tested, it was found to bring about a definite lysis of the cultures in three hours, but by this time the spinal fluid was already bacteria-free, and this phage was not used in therapy. Dr. Myers wrote to us on Jan. 4, 1935 to say that the patient was in perfect health without sequelae. He believed that the bacteriophages had no influence toward recovery and that the real turning point in the case was the complete drainage of the spinal canal incident to the taking of the encephalogram. Referring to the specific phage prepared in New York, he said: "The last phage did wonders in the laboratory, and should have helped, but the patient had recovered."

We have great respect for the opinion of the attending physician and the consultants in this case. However, the demonstration of the increasing amounts of agglutinins and precipitins in the spinal fluid suggests to us that an actual propagation of bacteriophage had become established in this spinal fluid by April 10, not adequate to cause complete solution of the bacteria but sufficient to induce phenomena of agglutination and precipitation. We have had occasion to observe phenomena of this sort in other patients treated with bacteriophages. Perhaps the introduction of the air may have served to secure a more complete distribution of

the bacteriophage throughout the cerebrospinal fluid. It is, however, not easy to believe that such a procedure alone could exert a beneficent influence on the course of a staphylococcic infection of the meninges. Hence we are inclined to credit this recovery in large measure to the use of the bacteriophages.

CASE 2.—*Youth, aged 19 years; meningococcic meningitis, serum therapy, convalescent; then diffuse staphylococcic meningitis, treated by intravenous, intraspinal and intracisternal injection of bacteriophage; recovery without sequelae.*

Another patient who recovered, H. D., a youth of 19, was admitted to St. Elizabeth's Hospital, New York, on Oct. 22, 1936. Diffuse staphylococcic leptomeningitis developed as a sequel to meningococcic meningitis. His abbreviated clinical chart has already been published.[3] Here it will suffice to say that all requirements for diagnosis were abundantly met in this case and that recovery followed the repeated intravenous, intraspinal and intracisternal injection of bacteriophage, without the use of any chemotherapeutic agents.

CASE 3.—*Man, aged 33 years; removal of tumor of brain; staphylococcic meningitis with general infection of leptomeninges; bacteriophage injected intravenously and also into site of cerebellar wound; recovery.*

S. O., a man aged 33, was admitted to the Neurological Institute on Aug. 8, 1937, to the service of Dr. John E. Scarff, who provided us with the record. The patient had suffered from frontal headaches since March 1937 and since May had had morning dizziness. On July 4, while playing tennis, he became dizzy and collapsed. Since then he had been unsteady, with a tendency to reel and fall and with frequent forceful vomiting preceded by nausea. Since July 23 he had been bedridden. More recently diplopia when looking to the right and dysuria had developed. On his admission to the hospital his speech was sluggish, and there were bilateral papilledema and slow pulse. The details of preoperative study, although interesting, are not important for our present purpose. On August 16 a tumor nodule (hemangioblastoma) was removed from the right cerebellar hemisphere by an operation lasting from 7:30 a. m. to 3:00 p. m. The postoperative course was characterized by almost continuous complaints with the exception of one day, August 22. The important features of the clinical record are shown in figure 2.

On August 27 there was evident inflammation in the wound, and a specimen taken for culture at this time yielded a growth of Staph. aureus, recognized after twenty-four hours. On August 28 the temperature reached 104 F. A drain was inserted beneath the operative flap, and at 4:00 p. m. 10 cc. of stock staphylococcus bacteriophage was slowly administered by low gravity pressure through a needle inserted beneath the flap. A blood culture made on this day remained sterile, but a second culture from the wound confirmed the previous finding. Beginning in the afternoon of August 29, the bacteriophage was given intravenously, ordinarily 2 cc. twice daily until September 26, when its use was discontinued. The injection of 10 cc. at the site of the wound was repeated on August 30 and September 3. The fistulous opening closed on September 4. Progress was satisfactory until September 14. Then there were severe headache and a rise in temperature and on the next day repeated vomiting. A lumbar tap at 4:45 p. m., September 15, yielded an opalescent fluid with a cell count of 598 and a 2 plus reaction for globulin. Cultures yielded staphylococci, but there were only a few colonies on the plate cultures. It was deemed unwise to repeat the spinal tap, for fear that this procedure might favor further dissemination of the infection. On September 24

3. MacNeal, W. J.: Recent Developments in Bacteriophage Therapy, New York State J. Med. **41**:1531-1536 (Aug. 1) 1941.

a specimen of fluid was obtained by aspiration of the site of the wound in the occiput. Examination of this fluid revealed a cell count of 104 and a 2 plus reaction for globulin, and a culture was sterile. The patient was discharged on October 6. A specific bacteriophage was prepared for this patient but was not used. Under date of October 26, Dr. Scarff wrote: "We did not call for this particular bacteriophage simply because the bacteriophage with which you supplied us so quickly produced satisfactory change." On October 15 the patient was able to walk half a mile. He still had some headache, occasional dizziness on turning quickly and rare episodes of nausea.

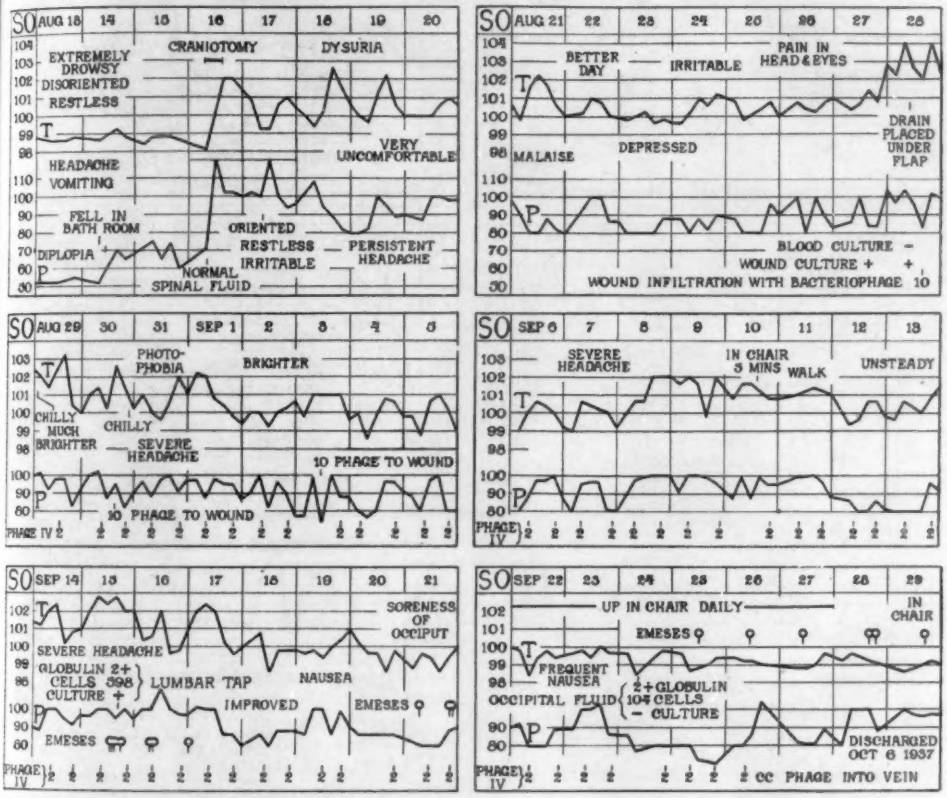

Fig. 2.—Abbreviated clinical chart of S. O. *T*, temperature; *P*, pulse rate.

CASE 4.—*Girl aged 16 years; staphylococcemia and diffuse staphylococcic leptomeningitis; bacteriophage given intravenously; recovery; record incomplete.*

J. C. (no. 391), a girl aged 16 years, was a private patient with a clinical diagnosis of meningitis and septicemia. We received a broth culture of a specimen of spinal fluid drawn on Jan. 27, 1939, and this was found to contain nonhemolytic Staphylococcus citreus and hemolytic Staphylococcus albus. A broth culture of spinal fluid drawn on January 31 was also sent to us and was found to contain the same two organisms. The agar plate of a blood culture, evidently made on January 31, was sent to us, and on this plate there were colonies of the same two

staphylococci. Specific bacteriophages active against both organisms were prepared. A blood culture made February 1 remained sterile. On February 2, the patient received a series of intravenous injections of stock staphylococcus bacteriophage to a total of 154 cc., after which she had a brief chill, and a rise in temperature with a subsequent fall. The injections of bacteriophage were continued, and on June 20, 1940 we learned that the patient had recovered. Unfortu-

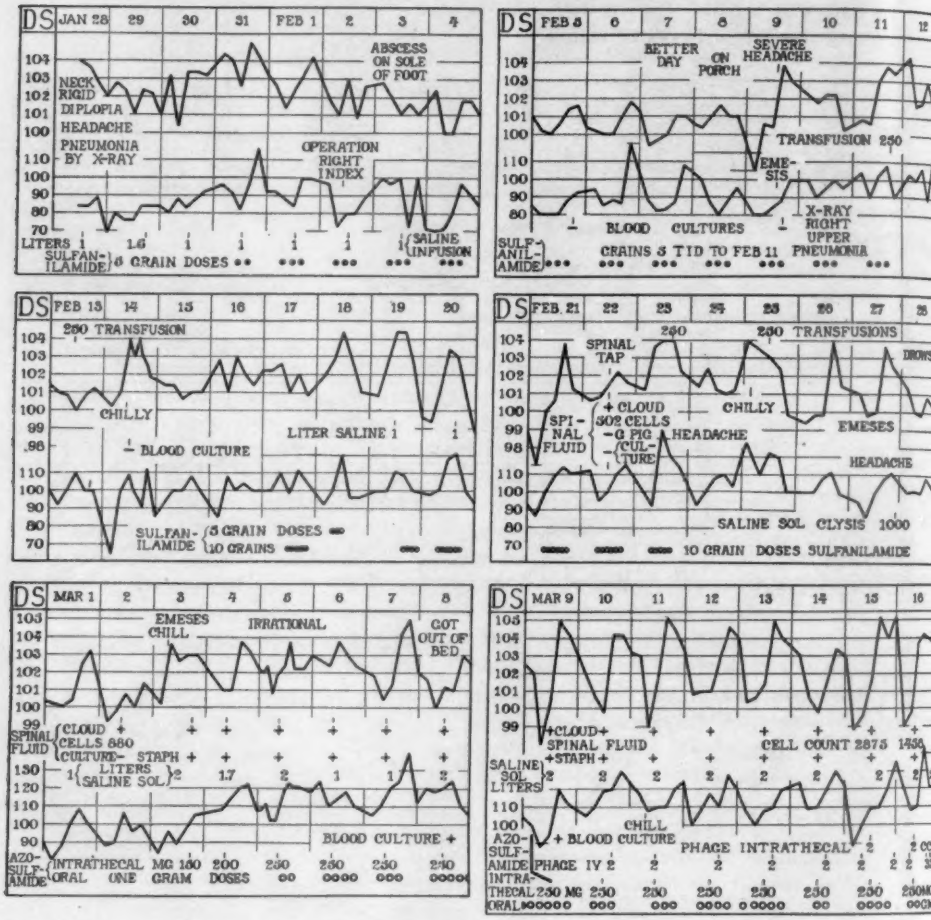

Fig. 3.—Abbreviated clinical chart of D. S. *T*, temperature; *P*, pulse rate.

nately it has been impossible to obtain a detailed clinical record of this patient, or indeed any further written information. Repeated requests over a period of many months elicited courteous promises that the record would soon be forthcoming and finally the reply that the record had been lost or destroyed and could not be supplied. Because of the presence of Staph. citreus in the cultures of the spinal fluid and of the blood we are inclined to consider these cultures valid and have therefore included this patient.

CASE 5.—*Youth, aged 18 years; staphylococcemia and staphylococcic meningitis; sulfanilamide given by mouth and azosulfamide by mouth and by intrathecal injection; positive cultures of spinal fluid and of blood; bacteriophage given by intrathecal and intravenous injection; treatment with sulfapyridine; relapse; again intravenous injection of bacteriophage; recovery without sequelae.*

D. S. (no. 402), a youth aged 18, was admitted in care of Dr. Vito Luongo to the Carson C. Peck Memorial Hospital of Brooklyn on Jan. 28, 1939, suffering

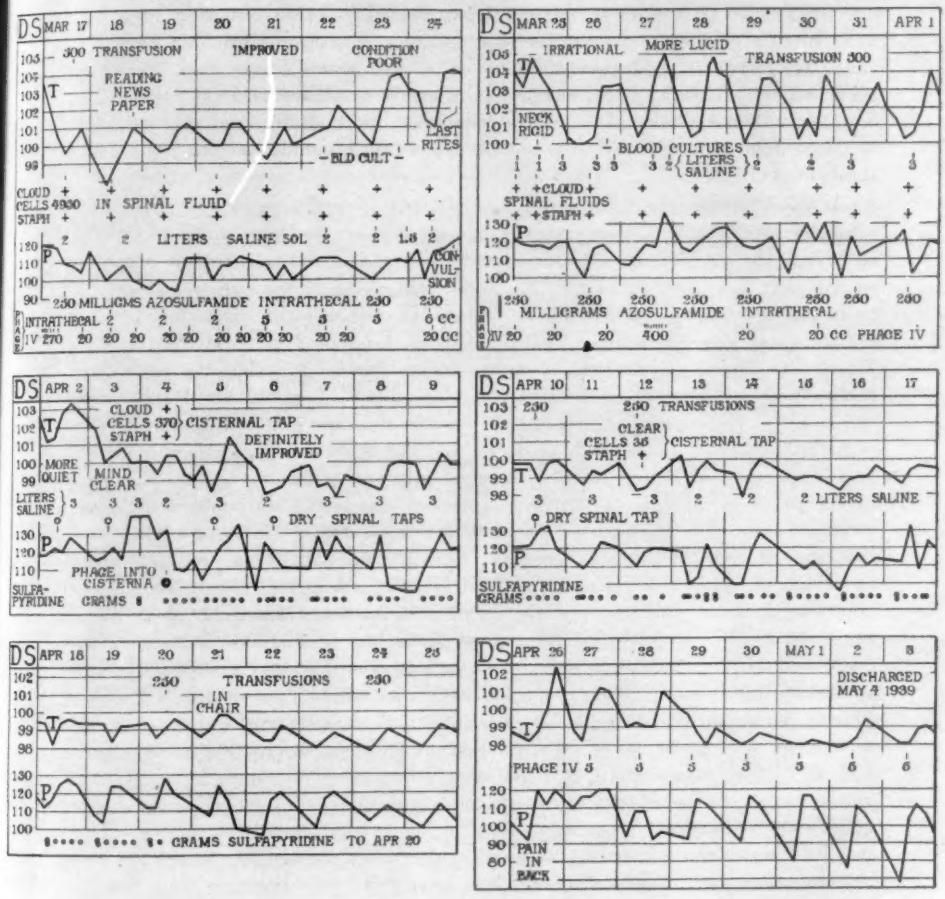

Fig. 3.—Continued

from headache, cough, diplopia, nuchal rigidity, fever and malaise, with a history of onset on January 18. A diagnosis of pneumonia was confirmed by roentgenologic examination. The abbreviated clinical chart, figure 3, shows the records of temperature and pulse and also the most important facts recorded during the course of this illness from January 28 to May 3. On admission to the hospital there was stiffness of the neck and strongly positive Kernig and Babinski signs, believed to be due to encephalitis. Physiologic solution of sodium chloride was given subcutaneously daily for the first week. On February 2 the nail was

removed from the right index finger to drain an abscess containing staphylococci. Sulfanilamide was given by mouth from January 31 to February 11 and again later as indicated in the chart. A spinal tap on February 22 yielded a cloudy fluid with cell count of 502. The culture of this fluid remained sterile, and a guinea pig inoculated with it remained well. The second spinal tap, done on March 2, gave no additional information. The cell count had increased to 802, but again the culture was sterile. However, the specimens of spinal fluid drawn daily from March 3 to April 1, inclusive, all yielded Staph. aureus. Possibly the interruption of sulfanilamide therapy from February 24 to March 3 may have facilitated the diagnosis. At any rate, azosulfamide (disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3'-6'-disulfonate) was used, treatment being begun on March 3 by intrathecal injection and continued on March 5 by oral administration also. The patient continued to do badly, and the specimens of spinal fluid, although definitely colored by the azosulfamide, persisted in yielding staphylococci in cultures.

A blood culture made on March 8 was reported sterile on March 9, but subsequently this culture showed a growth of staphylococci and was finally so reported on March 15. Another blood culture, made on March 9, also showed the organisms on the next day, with 6 colonies per cubic centimeter of the patient's blood. As soon as this growth in the blood culture became evident, bacteriophage was obtained and was given intravenously in daily doses of 2 cc. from March 10 to March 14. There was no evident improvement. During this time the use of azosulfamide was continued by mouth and by intrathecal injection. On March 15 the cell count of the spinal fluid was 2,875. At this time the first intrathecal injection of bacteriophage, 2 cc., was administered, and this dose was repeated on March 16. In the afternoon of March 16 an intravenous injection of 2 cc. of bacteriophage was given, and at 8:20 p. m. a series of injections was begun and continued through the night until at 8:15 a. m. on March 17 a total of 300 cc. had been administered. The clinical improvement was dramatic, such that the patient was able to read the newspaper on March 18. The spinal fluid, however, continued cloudy and cultures continued to show staphylococci. Blood cultures made on March 22, 23, 25 and 26 remained sterile. Nevertheless the patient again lost ground, and a progress note on March 23 said, "Seems to have fallen back to where he was a week ago, before treatment with phage." That night he was irrational and got out of bed, and on March 24 an intrathecal injection of 250 mg. of azosulfamide and 6 cc. of bacteriophage was given at 10:00 a. m. At 6:30 p. m. he got out of bed again, and at 9:00 p. m. there was a convulsion lasting seven minutes. Last rites were administered. A second series of intravenous injections of bacteriophage was given on March 27 from 11:15 a. m. to 9:00 p. m., a total amount of 400 cc. There was no distinct reaction, but the patient's temperature reached 105 F. at 8:00 p. m., and the next day he was distinctly less irrational. The situation was, however, very discouraging. Azosulfamide, 250 mg. daily, was given intrathecally from March 23 to April 1, inclusive, during which time there was little evidence of favorable progress. No bacteriophage was given on March 31, April 1, 2 or 3, and the azosulfamide was last given on April 1. On April 2 and 3 there was apparent clinical improvement. Spinal taps on these days failed to obtain any fluid, and so on April 4 a cisternal tap was done by Dr. Josephine Neal. A slightly cloudy fluid which had a cell count of 370 and yielded staphylococci on culture was obtained. At this time bacteriophage was injected into the cisterna. The record does not give the amount. It says "45 cc. fluid withdrawn, bacteriophage solution replaced."

Sulfapyridine was given from about midnight April 3 to the morning of April 20. During this time the patient seemed decidedly improved. Spinal taps were dry on April 5, 6 and 10, but cisternal tap on April 12 yielded a fluid which, although clear, nevertheless still contained an excess of cells and also yielded staphylococci on culture. On April 26 there was a relapse with pain in the back and rise in temperature to 102.4 F. Bacteriophage was given intravenously, 5 cc. daily from April 27 to May 3. On May 4 the patient was discharged in excellent condition, without any evidence of sequelae. Injections of bacteriophage were continued at home. On July 10, 1939 he came to see us for the first time, bringing a note from Dr. Luongo, as follows: "Introducing D—— S——, who was as close to the pearly gates as any one ever gets and is now convalescing splendidly. Will you kindly let him have another supply of staph phage? Warm thanks."

Dr. Luongo, who supplied the clinical record of this patient, cooperated faithfully throughout, and Dr. Josephine Neal showed unremitting zeal as clinical consultant in a desperate and difficult situation.

CASE 6.—*Man 41 years of age; neurosyphilis; diffuse staphylococcic leptomeningitis, following lumbar tap; bacteriophage given by intravenous and intrathecal injection; recovery.*

W. R., a man aged 41 suffering from neurosyphilis, was admitted to the University Hospital, Ann Arbor, Mich., on Aug. 23, 1939. He passed through a desperate attack of staphylococcic meningitis in the period August 24 to September 20, during which time he was treated by intravenous and intrathecal injections of bacteriophage. On September 20 the Lange colloidal gold curve was essentially the same as it had been on August 24, before the onset of the staphylococcic infection. This recovery has been reported by the clinicians [4] who cared for the patient. The bacteriophage was supplied from our laboratory.

CASE 7.—*Woman 63 years of age; craniotomy for tic douloureux; localized meningitis; sulfathiazole given by mouth and by subcutaneous injection to limit of tolerance; extension of infection to produce diffuse leptomeningitis; eventually specific bacteriophage given by intravenous and intrathecal injection; recovery with partial disability.*

K. V., a woman aged 63, who suffered from intractable recurrent tic douloureux, was admitted to the Albany Hospital, service of Dr. Albert M. Yunich, on July 15, 1940, and on the following day craniotomy with section of the trifacial nerve was performed. There was postoperative fever, which did not cause grave concern until July 24, when stiffness of the neck became manifest. Spinal puncture revealed a cloudy fluid, containing 6,000 white cells per cubic millimeter. Administration of sulfathiazole by mouth, 4 Gm. every four hours, was immediately started at 5:00 p. m. on July 24 and continued until the patient vomited at 9:00 a. m. July 25, when the dose was somewhat reduced, as indicated in the graphic chart. After a total amount of 55 Gm. had been given, this drug was discontinued on July 28. Cultures of the fluid obtained by lumbar tap on July 24, 25 and 27 remained sterile, indicating that the staphylococci demonstrated at the operative site were not able to overcome the protective inflammatory barriers and proliferate in the generally circulating cerebrospinal fluid. The spinal fluid on

4. MacNeal, P. S., and Foster, D. B.: Two Cases of Staphylococcic Meningitis Treated with Asparagin Bacteriophage, Am. J. M. Sc. **202**: 874-879 (Dec.) 1941.

July 25 contained 1.7 mg. of free sulfathiazole and a total of 1.9 mg. of the drug per hundred cubic centimeters. The level of the drug in the circulating blood was about three times higher.

After the use of sulfathiazole was discontinued, on July 28, the patient seemed better, and the possibility of toxic fever due to the drug was suggested. The drain was removed from the cranial wound on July 31. Culture of the exudate again showed Staph. aureus. The temperature and pulse rate rose again rather promptly, and early on August 2 the neck became stiff. A second course of sulfathiazole was started with 4 Gm. at 11:00 a. m. August 2 and continued to 7:00 a. m. August 4, when a total of 42 Gm. had been administered. Some of this was given in dilute form by hypodermoclysis. On August 3 multiple papules appeared on the skin, which were thought to be furuncles. A blood culture was made on this day, and an intravenous injection of 1 cc. of stock staphylococcus bacteriophage was given at about 11:00 p. m. On the following morning the eruption was recognized as probably a drug rash, and the administration of sulfathiazole was discontinued at this time. The rash faded promptly, and the patient improved in a gratifying manner. On August 13 there was an ominous aggravation of pain in the lumbar region, and on August 15 the neck was slightly stiff. Nevertheless the patient was permitted to sit up in bed and to dangle her feet. Lumbar puncture on August 16 yielded a spinal fluid with only 675 cells per cubic millimeter, which was sterile on culture. Small transfusions, of 150 cc. each, were given on August 16, 17 and 19. The patient walked a few steps on August 22. On the next day she became incontinent of urine and feces, the neck became rigid and the temperature rose sharply to 103 F. At 7:00 p. m. the skin over the cranial defect was tense without evident pulsation and neurologic signs of meningeal irritation were more pronounced. The cranial wound was explored with the area under local anesthesia. The diagnostic dural taps gave negative results. Spinal punctures were done at the level of the twelfth vertebra thoracic and the first, fourth and fifth lumbar vertebrae, and cloudy fluids were obtained. The specimen from the upper level gave a count of 1,462 cells per cubic millimeter and that from the lower level a count of 1,498. An average figure of 1,480 is shown on the graphic chart on August 23. Culture of these fluids yielded a growth of Staph. aureus, thus for the first time supplying evidence of general dissemination of the infection to the circulating cerebrospinal fluid. A third course of sulfathiazole was started at once, with a dose of 3 Gm. at 11:00 p. m. Lumbar taps on August 24 and 26 revealed cocci in the microscopic examination of smears. On August 26 the end seemed near, as indicated by the progress note: "Patient has failed rapidly with this exacerbation, which commenced three days ago, after an asymptomatic period of exactly one week. This was the first time that a frank purulent diffuse meningitis with probably multiple subarachnoid abscesses could be demonstrated. Direct smears of the spinal fluid revealed large numbers of staphylococci, and on culture these have proved to be of the aureus type. In spite of relatively large doses of sulfathiazole, fluids and small transfusions, the patient has become progressively worse. At present she shows signs of profound toxemia—cardiac rate 144; temperature 103.6 F.; respiratory rate 32 and breathing labored; extremities cold and moist; face flushed; patient comatose; no response except to painful stimuli; prognosis very grave." The level of sulfathiazole in the blood at this time was 5.5 mg. per hundred cubic centimeters. The dose was now reduced. Two days later, August 28, this note was made: "General condition improved; vital signs almost normal except for moderate tachycardia; erythematous maculopapular drug rash has reappeared on neck, upper part of chest and upper part of arm; injection of right sclera and

conjunctiva marked. In addition to these toxic signs from sulfathiazole, the patient also exhibits slight confusion and disorientation for time and place and has definite visual hallucinations. Because of the increasing toxic manifestations from the drug its use is being temporarily suspended and it will be administered cautiously after a discreet interval."

There followed a period of encouraging behavior until September 6, when cervical rigidity and mental stupor appeared about midnight. Lumbar tap on the morning of September 7 yielded 35 cc. of staphylococcic pus, which became more liquid toward the end of flow. The skin over the cranial defect was tense and hard at this time. Because of nausea, vomiting and especially the reappearance of the rash on September 10 the use of sulfathiazole was discontinued on this day. Stock bacteriophage was injected intravenously, 1 cc. on September 12, 2 cc. each morning and evening on September 13 and 14 and 2 cc. on September 15. On the morning of September 15 spinal tap yielded 6 cc. of purulent fluid, and 2 cc. of the stock phage was injected into the spinal canal. Some of this infected spinal fluid was mixed with the bacteriophage and incubated in a test tube over night. Subculture from this mixture gave positive growth, and this result was considered evidence of inefficiency of the stock bacteriophage. Its use was therefore discontinued, and a culture was sent to the Post-Graduate Hospital in New York for preparation of a specific bacteriophage. Sulfathiazole was again administered in small doses.

Spinal taps on September 18, 20, 23 and 25 continued to show turbid purulent fluid with viable staphylococci present. On September 20 the spinal canal was irrigated with a 0.1 per cent solution of sodium sulfathiazole. At this time some of the spinal fluid was mixed with sulfathiazole and the mixture incubated. Subcultures of this mixture after three and six hours revealed little if any bactericidal effect, "much to our surprise" (quoted from bedside progress note). The administration of sulfathiazole was discontinued on September 23, and no more of this agent was used. The specific bacteriophage was given intravenously in doses of 2 cc., beginning on September 21 and with fair regularity twice daily until Dec. 1, 1940. Laboratory tests of this specific bacteriophage showed it to be about a thousand times more potent against the patient's staphylococcus than was the stock phage previously used. On September 23 this specific phage was employed for spinal irrigation. A mixture of the purulent spinal fluid with the phage was incubated in the test tube. After twenty-four hours staphylococci were present, but after forty-eight hours the organisms were completely lysed and subculture gave a negative result. The clinical condition seemed better, and the temperature did not again exceed 99 F. after September 23. Nevertheless, the spinal fluid obtained on September 25 was still turbid and yielded growth of staphylococci. Again the spinal canal was irrigated with bacteriophage, and 5 cc. was allowed to remain. On September 27 a lumbar tap under general anesthesia failed to obtain any fluid. Some eight hours later there were paresis of the legs and incontinence. On October 9 there was a complicating pyuria due to infection with colon bacilli.

A thorough examination on December 10 disclosed some persistent neurologic defects. The left corneal reflex was absent (fifth nerve sectioned). The left pupil was larger than the right, but both reacted normally to light. The legs were markedly atrophic, and the left leg was flaccid with impaired sense of position. The patient was able to walk with aid of a nurse. Sphincter tone had been partially regained. She was discharged from the hospital at 1:55 p. m. Dec. 11, 1940.

The most important features of this case record are shown in the graphic chart, figure 4. The frequent administration of fluid and solutions of sodium chloride and dextrose by subcutaneous and intravenous routes has not been shown because of limitations of space, but it should be noted that adequate fluid intake was maintained by this means throughout the course of the illness.

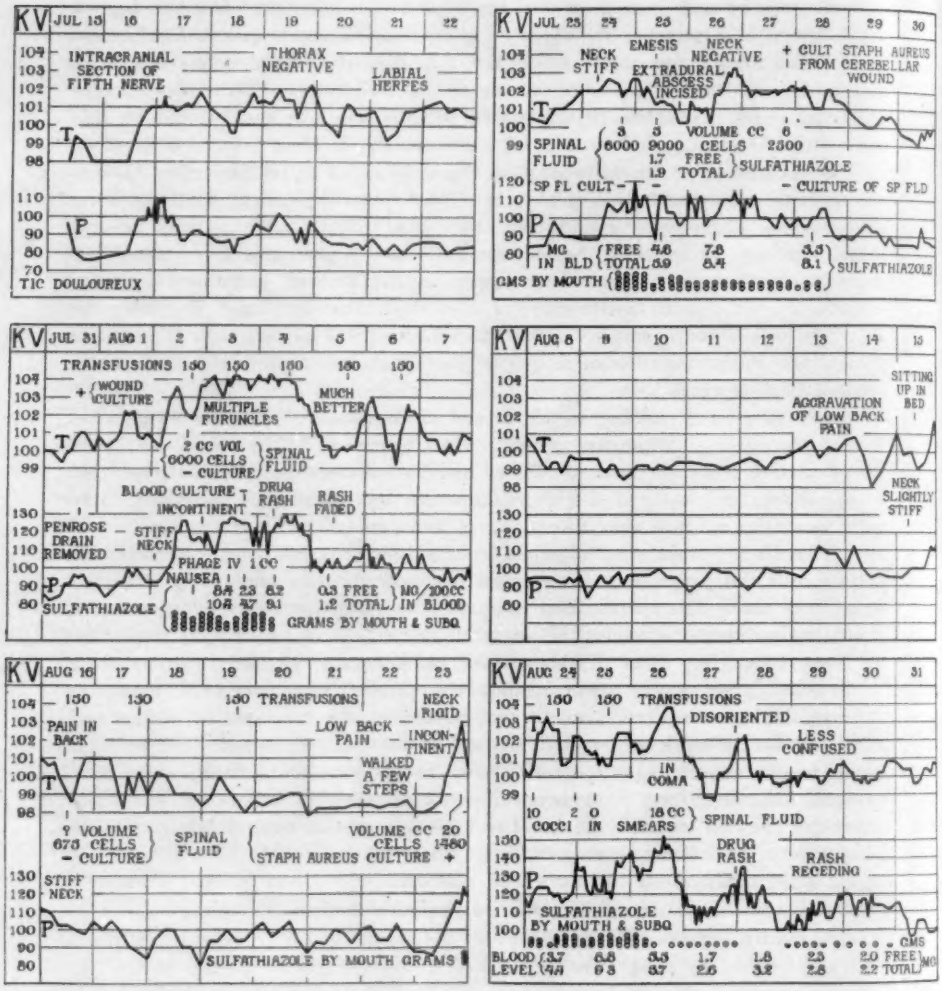
KV
JUL 15 16 17 18 19 20 21 22
INTRACRANIAL SECTION OF FIFTH NERVE
THORAX NEGATIVE
LABIAL HERPES
TIC DOULOUREUX
JUL 25 24 25 26 27 28 29 30
NECK STIFF
EMESIS
NECK NEGATIVE
+ CULT STAPH AUREUS FROM CEREBELLAR WOUND
EXTRADURAL ABSCESS INCISED
SPINAL FLUID
VOLUME CC 6
6000 9000 CELLS 2500
1.7 1.9 FREE TOTAL
SULFATHIAZOLE
SP FL CULT - -
- CULTURE OF SP FLD
MG IN BLD FREE 4.6 7.8 3.5 TOTAL 5.9 8.4 6.1
SULFATHIAZOLE
GMS BY MOUTH
JUL 31 AUG 1 2 3 4 5 6 7
TRANSFUSIONS 150 150 150 150 150
WOUND CULTURE +
MULTIPLE FURUNCLES
MUCH BETTER
2 CC VOL 6000 CELLS - CULTURE
SPINAL FLUID
BLOOD CULTURE + INCONTINENT
DRUG RASH
RASH FADED
PENROSE DRAIN REMOVED
STIFF NECK
PHAGE IV 1 CC
NAUSEA
SULFATHIAZOLE
8.4 2.3 6.2 10.8 4.7 9.1
0.3 FREE 1.2 TOTAL
MG/100CC IN BLOOD
GRAMS BY MOUTH & SUBQ
AUG 8 9 10 11 12 13 14 15
SITTING UP IN BED
AGGRAVATION OF LOW BACK PAIN
NECK SLIGHTLY STIFF
AUG 16 17 18 19 20 21 22 23
150 150 150 TRANSFUSIONS
NECK RIGID
PAIN IN BACK
LOW BACK PAIN
INCONTINENT
WALKED A FEW STEPS
? VOLUME 675 CELLS - CULTURE
SPINAL FLUID
VOLUME CC 20 CELLS 1480 STAPH AUREUS CULTURE +
STIFF NECK
SULFATHIAZOLE BY MOUTH GRAMS
AUG 24 25 26 27 28 29 30 31
150 150 TRANSFUSIONS
DISORIENTED
LESS CONFUSED
IN COMA
10 2 0 18 CC COCCI IN SMEARS
SPINAL FLUID
DRUG RASH
RASH RECEDING
SULFATHIAZOLE BY MOUTH & SUBQ
GMS
BLOOD LEVEL 3.7 4.8 5.8 9.3 5.5 8.7 1.7 2.6 1.8 3.2 2.5 2.8 2.0 FREE 2.2 TOTAL MG

Fig. 4.—Abbreviated clinical chart of K. V. *T*, temperature; *P*, pulse rate.

The careful clinical and laboratory studies leave no doubt that here is an example of focal intracranial infection with Staph. aureus which remained fairly well localized for several weeks, July 16 to August 23. The inflammation appeared to be somewhat controlled by sulfathiazole, but the patient was evidently unable to take large amounts of this drug without serious toxic effects, which approached a terminal stage on August 26. Those who are enthusiastic about bacteriophage

may consider it unfortunate for the patient that the use of phage was not continued on August 4. However, this has probably contributed to the teaching value of the case. Certainly the sulfathiazole was given a thorough trial, and it undoubtedly did much to prevent an early fatal termination. The improvement which was associated with the administration of stock bacteriophage, September 12 to 15, became little short of dramatic when the specific bacteriophage was given by intravenous injection and by intrathecal irrigation, September 22 and thereafter. Under the drug therapy the disease was partly controlled, but in spite of that the

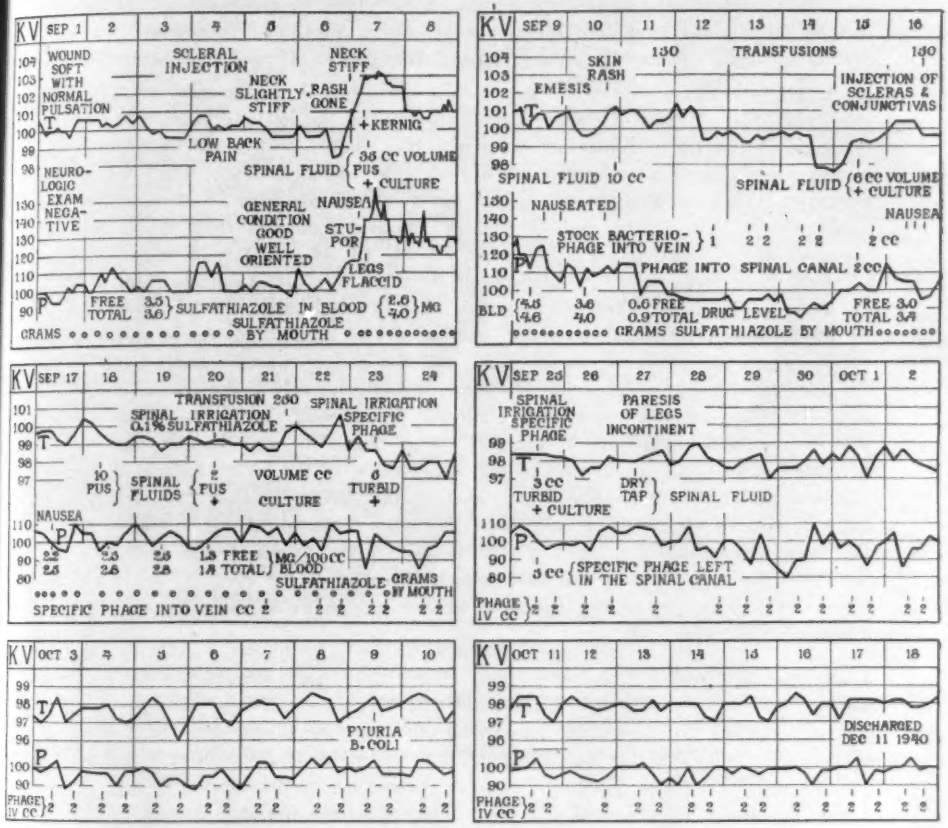
KV
SEP 1 2 3 4 5 6 7 8
WOUND SOFT WITH NORMAL PULSATION
SCLERAL INJECTION
NECK SLIGHTLY STIFF
NECK STIFF
RASH GONE
+ KERNIG
LOW BACK PAIN
SPINAL FLUID 35 cc VOLUME PUS + CULTURE
NEUROLOGIC EXAM NEGATIVE
GENERAL CONDITION GOOD WELL ORIENTED
NAUSEA
STUPOR
LEGS FLACCID
FREE 3.5 TOTAL 3.6 SULFATHIAZOLE IN BLOOD 2.6 4.0 MG
SULFATHIAZOLE BY MOUTH
GRAMS
KV
SEP 9 10 11 12 13 14 15 16
SKIN RASH
EMESIS
130
TRANSFUSIONS
130
INJECTION OF SCLERAS & CONJUNCTIVAS
SPINAL FLUID 10 cc
SPINAL FLUID 6 cc VOLUME + CULTURE
NAUSEATED
NAUSEA
STOCK BACTERIOPHAGE INTO VEIN 1 2 2 2 2 cc
PHAGE INTO SPINAL CANAL 2 cc
BLD 4.5 4.6 3.6 4.0 0.6 FREE 0.9 TOTAL DRUG LEVEL FREE 3.0 TOTAL 3.7
GRAMS SULFATHIAZOLE BY MOUTH
KV
SEP 17 18 19 20 21 22 23 24
TRANSFUSION 250
SPINAL IRRIGATION 0.1% SULFATHIAZOLE
SPINAL IRRIGATION SPECIFIC PHAGE
10 PUS SPINAL FLUIDS 2 FUS + VOLUME cc 6 TURBID + CULTURE
NAUSEA
2.5 2.5 2.6 2.6 1.3 FREE 1.4 TOTAL MG/100 CC BLOOD SULFATHIAZOLE GRAMS BY MOUTH
SPECIFIC PHAGE INTO VEIN cc 2 2 2 2 2 2
KV
SEP 25 26 27 28 29 30 OCT 1 2
SPINAL IRRIGATION SPECIFIC PHAGE
PARESIS OF LEGS INCONTINENT
3 cc TURBID + CULTURE
DRY TAP SPINAL FLUID
3 cc SPECIFIC PHAGE LEFT IN THE SPINAL CANAL
PHAGE IV cc 2 2 2 2 2 2 2 2 2 2 2 2 2 2
KV
OCT 3 4 5 6 7 8 9 10
PYURIA B. COLI
PHAGE IV cc 2 2 2 2 2 2 2 2 2 2 2 2 2 2
KV
OCT 11 12 13 14 15 16 17 18
DISCHARGED DEC 11 1940
PHAGE IV cc 2 2 2 2 2 2 2 2 2 2 2 2 2 2

Fig. 4.—Continued

local infection became generalized in the circulating cerebrospinal fluid on August 23. Evidently there was a secondary abscess in the lumbar region.

The 7 cases records of which have just been reviewed we regard as acceptable examples of recovery from staphylococcic diffuse leptomeningitis. Two of the 7 reports have been previously published and have been included in our list of the 48 acceptable cases. The present report, therefore, adds 5 more, bringing the total of acceptable recoveries to 53.

We also shall include here 4 other cases. Two of the patients, A. D. and D. B. (no. 480), have already been discussed in the papers dealing with thrombosis of the cavernous sinus. The cases of the 2 remaining patients, S. W. and H. C., were examples of localized meningitis not previously recorded.

CASE 8.—*Woman aged 26; thrombosis of cavernous sinus; ligation of jugular vein; treatment with azosulfamide; evisceration of orbit; meningitis; staphylococcemia; bacteriophage given by intrathecal injection, by irrigation of the orbit and by intravenous injection; subsidence of clinical signs and symptoms; patient discharged home; subsequent postoperative death; abscess of cerebellum at autopsy.*

A. D. (no. 294), a woman aged 26, was admitted to the hospital on Oct. 7, 1937 with clinical signs of septic thrombophlebitis of the left cavernous sinus and meningitis. The left common carotid artery was ligated on the day of admission and treatment with azosulfamide instituted. On October 9 the left orbit was eviscerated and the thrombosed ophthalmic vein was identified. Blood cultures made on October 11, 15 and 19 yielded staphylococci, and cultures of specimens of spinal fluid taken on October 10, 11, 13, 14, 15, 16, 23 and 24 also revealed these organisms. Beginning on October 17, bacteriophage was given by intrathecal injection and by irrigation of the eviscerated left orbit and later by intravenous injection at irregular intervals. The spinal fluid ceased to reveal staphylococci in culture on October 26, and the patient was discharged on Jan. 29, 1938, apparently convalescent. However, she subsequently died on April 2, 1938, after cerebellar decompression, and at autopsy a cerebellar abscess was found near the midline and extending to the left. The record of this patient has been presented elsewhere [5] in greater detail, together with the chart record of temperature and pulse rate. She is included in this group because the meningitis actually cleared up under bacteriophage therapy. We are inclined to the opinion that a more regular and more persistent use of the bacteriophage might have protected the patient from the fatal sequel. Because of the eventual death from cerebellar localization of the infection we are unable to accept this case as an example of recovery.

CASE 9.—*Boy aged 12 years; nasal sepsis; operation on right antrum and right frontal sinus; staphylococcemia; thrombosis of cavernous sinus; treatment with sulfapyridine; nuchal rigidity; bacteriophage given by intravenous injection and by local application to wounds; visual disturbances and recurrent nuchal rigidity; gradual recovery.*

D. B. (no. 480), a boy of 12 years, admitted to the hospital on Jan. 7, 1940, has been reported on in our series of recoveries from staphylococcic septic thrombosis of the cavernous sinus,[5] and his abbreviated clinical chart has been included in this earlier report. After the patient seemed to be convalescing from his septic thrombosis, his fever returned on January 26 and there were visual disturbances, vomiting and nuchal rigidity. Spinal tap was not done, and these alarming symptoms and signs disappeared. The patient was discharged on Feb. 18, 1940, in good condition. Subsequent information is lacking. Considering the earlier record of this patient, it seems very probable that a localized meningitis was present in the period January 26 to 31, but the evidence does not permit acceptance of the case as an example of recovery from meningitis.

5. MacNeal, W. J.; Frisbee, F. C., and Blevins, A.: Bacteriophage Therapy of Staphylococcic Septic Obstruction of the Cavernous Sinus: II. Report of Cases, Arch. Ophth. **29**:341-368 (March) 1943.

CASE 10.—*Woman aged 38; laminectomy in cervical portion of spine; postoperative suppuration of wound; drainage; bacteriophage given locally and intravenously; slow recovery.*

S. W., a woman aged 38, was admitted to the New York Post-Graduate Medical School and Hospital on Jan. 21, 1935, complaining of pain in the right side of the head and face, which had persisted since April 1934. On Jan. 26, 1935, with the patient under anesthesia induced with avertin with amylene hydrate, a spinal laminectomy was performed, the spines and laminas of the first five cervical vertebrae. The dura mater was incised from the level of the fourth cervical segment up to the foramen magnum. The sensory roots of the first, second and third cervical nerves were divided, and the dural incision was closed with a continuous suture of black silk, the muscle layer with interrupted chromic catgut and the subcutaneous tissues and skin with interrupted black silk. The operation required four and a half hours. Subsequent to this operation there was a gradual rise in temperature. On January 31 the operative wound was reopened. The skin and subcutaneous tissues appeared normal. On division of the muscle layer, however, there was an escape of 2 to 3 cc. of thick pus coming chiefly from the vicinity of the foramen magnum. Culture of this gave a pure growth of Staph. aureus. All the sutures were removed from the muscle, this freely exposing the dura mater, which was not touched by hand or instrument. No irrigation was employed. The wound was loosely packed with petrolatum gauze covered with a retaining dressing. The condition of the patient improved promptly. The packing was completely removed on February 1 and new petrolatum gauze inserted. On February 2 the outer dressing was renewed. At 1:30 a. m. February 3 the patient complained of pain in the chest and neck and numbness of the legs. The respirations were at a rate of 40 per minute and labored. There were profuse diaphoresis and considerable drainage from the wound. The dressing was changed daily from February 3 to February 8. The purulent exudate continued to be abundant, but fortunately the sutured dura seemed to prevent deeper extension of the inflammation.

At 1:30 p. m. on February 8 an intravenous injection of 1 cc. of bacteriophage was administered, and the wound itself was irrigated with bacteriophage. On February 9 the intravenous dose was repeated, and the bacteriophage was applied to the wound on saturated absorbent cotton for a period of one hour. This procedure was continued daily. On March 16 the patient was allowed to sit in a chair; on March 20 she walked alone, and on April 30 she was discharged from the hospital. She continued to be treated with bacteriophage as an outpatient until July 6, 1938, at which time the suboccipital sinus had finally healed. The patient was last seen in December 1940, when she was examined in the gynecologic clinic, the neurologic clinic and the goiter clinic. At this time the following recommendations were made: (1) that the patient be permitted rest and economic security for at least six months, and (2) that she continue to take vitamin B.

CASE 11.—*Man aged 37 years; plastic craniotomy for jacksonian epilepsy; staphylococcic infection of the craniotomy wound; surgical drainage; injection of bacteriophage into site of wound and intravenously; recovery.*

H. C., a man aged 37, was admitted to the hospital on Dec. 4, 1938 for a plastic operation on his skull. In 1908 he had suffered a fracture of the skull caused by the crank handle of a motor car. He received another head injury in 1930, and since that time he had approximately four jacksonian seizures each year with a tendency to increased frequency to eight per year. The attacks were preceded by an aura, with twisting of the eyes to the right, followed by a cry,

unconsciousness, headache and sleep. In 1932 he had a plastic repair of the right frontal bone, and he was then free from attacks for about two years. Then they returned, again about eight a year.

On March 1, 1937 an encephalogram revealed asymmetric dilatation of the lateral ventricles without distinct change in the third ventricle. There was a large collection of air over the left anterior cerebral area at the site of the old operative procedure, with suggestion of cortical atrophy.

Following this examination the attacks recurred at intervals of about six weeks. On Jan. 7, 1938 another encephalogram was made. After this there were nausea and vomiting and slightly elevated temperature for ten days. The epileptic attacks continued at about the same frequency, but with briefer aura.

On Dec. 5, 1938, about noon, a plastic operation on the skull was performed. The wound flap was swollen on the next day, and aspiration released 30 cc. of pink fluid. On December 7 the flap was incised and a rubber drain inserted. Abundant serous spinal fluid escaped. At 10:00 p. m. the drain was removed, and there was a gush of fluid. This fluid contained leukocytes, 78 per cent polymorphonuclears, and a culture yielded growth of Staph. aureus, recognized on December 8.

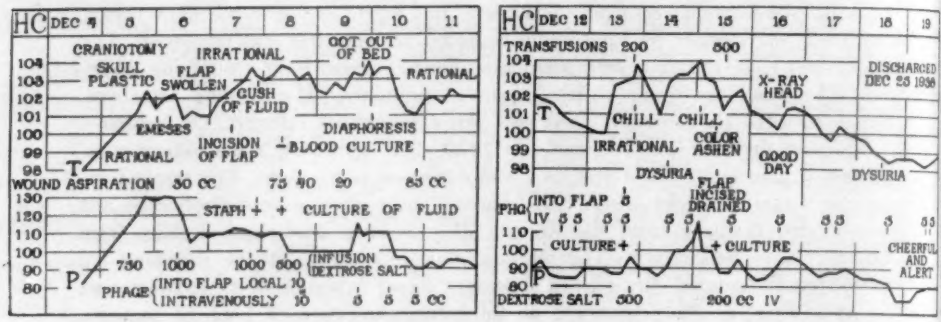

Fig. 5.—Abbreviated clinical chart of H. C. *T*, temperature; *P*, pulse rate.

On this day aspiration removed 40 cc. of fluid and 10 cc. of stock staphylococcus bacteriophage was injected under the flap and three intravenous injections (totaling 10 cc.) were given. The intravenous doses were continued as shown in the abbreviated clinical chart, figure 5, usually 5 cc. once or twice daily with omission on December 11. The injection into the wound flap was repeated on December 13. The patient was disoriented and at times difficult to control on December 7, 8 and 9, and there was frequent twitching of hands and feet, especially on the left side. The eyelids were very edematous. On December 10 the patient became rational and checked on the day of the month, the date of his operation and the number of his hospital room. Noticeable tremor of the hands persisted. On December 13 there was a serious relapse, which continued to be alarming until December 16. Then there was steady improvement. The last injection of bacteriophage was given on December 20. The patient was allowed out of bed on December 23 and was discharged on December 25. Continuing inflammation in the scalp wound was treated by local revision of the wound on May 23, 1939, with uneventful convalescence and discharge from the hospital on June 7, 1939.

There is no evidence that the meningitis had become generally disseminated in this case, but there can be no doubt that a dangerous local staphylococcic meningitis was present as a complication of the craniotomy. The neurosurgeon, Dr. J. Arthur MacLean, permitted us to use the records for this patient.

COMMENT

In this group of 7 acceptable recoveries from staphylococcic meningitis and 4 cases which, for indicated reasons, have been unacceptable, there is 1 example of accidental fracture of the skull with loss of brain substance (patient W. G., aged 7 years). The scalp wound healed within three weeks, but a diffuse staphylococcic meningitis was revealed by spinal puncture at the beginning of the third week and persisted for four weeks. Intrathecal injections of three different bacteriophage preparations were given, the last on April 9. After this date the bacteria in the spinal fluid behaved in a peculiar manner, tending to clump and precipitate, and after ventriculography on April 13 there was rapid convalescence.

There are 3 examples of staphylococcic meningitis following craniotomy, in 1 of which the inflammation evidently remained fairly well localized (H. C.). While the clinical result following bacteriophage therapy was highly satisfactory in this case, it is recognized that recovery might have been expected without use of this therapeutic agent. In the case of S. O. the staphylococcic infection extended throughout the subarachnoid space and the beneficial influence of the bacteriophage seems distinctly evident. Probably drainage through the occipital wound was also favorable in the earlier weeks, but this was not a factor after September 4, because the fistulous opening was no longer present. The last of the 3 patients, K. V., has a most valuable record. In her case the diffuse staphylococcic meningitis was evidently kept under control to a considerable extent by use of sulfathiazole to the limit of tolerance and eventually, when the bacteriophage was administered intravenously and intrathecally, the infection was speedily overcome.

The 1 example of peripachymeningitis following cervical laminectomy and dural incision (S. W.) illustrates the possibility of complete healing after the deep tissues of the neck, the cut surfaces of five cervical vertebrae and the external surface of the sutured dural incision had been bathed in staphylococcic purulent exudate. The recovery in this case required many months, as was indeed to be expected, considering the opportunity for extension of the infection into the epidural space and into the bony substance of the vertebrae.

These 5 cases of staphylococcic infection of gross wounds of the skull and vertebral column offer information which should be helpful to those surgeons who may be confronted with meningitis of this type, whether it has followed a war wound or an industrial or traffic accident or has developed as a postoperative complication. Recognition of the specific infectious microbe makes it possible to employ the therapeutic measures adapted to combat the particular infection. When the infectious microbe is a staphylococcus the help offered by staphylococcus bacteriophage should not be ignored.

In the group of 11 cases there are 2 in which staphylococcic infection evidently entered the meninges as the sequel to lumbar taps (H. D. and W. R.). In these the disease was a diffuse purulent leptomeningtis, and both are acceptable examples of recovery following intravenous and intrathecal injection of bacteriophage. The careful students of the problem of meningitis should not neglect to study the more detailed reports of these 2 cases, to which reference has been made earlier in this paper.

There are 2 examples of meningitis associated with septic obstruction of the cavernous sinus, both previously published. One of the patients (A. D.) had blood cultures and numerous cultures of the spinal fluid which yielded staphylococci and a surgically demonstrated septic clot in the ophthalmic vein, along with the classic clinical evidence of septic thrombosis of the cavernous sinus and diffuse purulent leptomeningitis. Bacteriophage was used to irrigate the eviscerated orbit, by intravenous and by intrathecal injection. Apparent recovery was followed by death from cerebellar abscess about six months after onset of the disease. We do not, therefore, accept this as an example of recovery. One can only regret that the bacteriophage therapy was not continued more vigorously in this case. The other patient with septic thrombosis of the cavernous sinus (D. B.) had only clinical evidence of meningitis, without spinal tap, and the follow-up record is inadequate. Hence this case is not acceptable as a valid instance of recovery from meningitis.

There are 2 examples of recovery from staphylococcic meningitis of cryptogenic or septic origin, 1 of which, the case of J. C., aged 16, is considered acceptable although the record leaves something to be desired. The other, the case of D. S., would appear fully acceptable. This patient was treated with sulfanilamide, azosulfamide, sulfapyridine and bacteriophage. The bacteriophage therapy was continued for a considerable time after the patient's discharge from the hospital in order to suppress recurrence of the meningitis or other sequelae.

When the malignant nature of staphylococcic meningitis until recent times is considered, it must be recognized that a forward step has been taken in dealing with this disease. We believe that recovery may sometimes be achieved even from diffuse staphylococcic meningitis associated with staphylococcemia and thrombosis of the cavernous sinus by the use of bacteriophage alone or by the use of a sulfonamide compound (especially sulfathiazole or sulfapyridine) alone. However, we do not think that the physician who is confronted with such a desperate therapeutic problem should fail to give his patient the benefit of both a sulfonamide compound and bacteriophage. The use of antitoxic serum should also be considered. In general one may expect to exhaust the usefulness of the serum in a week, and the wisdom of continuing the use of the sulfonamide compound after the second week may well be questioned.

There is, however, in our opinion, no shadow of excuse for discontinuing treatment with the bacteriophage until at least three months after all signs and symptoms of active infection have disappeared. The possibility of latent intracranial sequelae must always be kept in mind after apparent recovery from staphylococcic meningitis.

SUMMARY

During ten years of bacteriophage service for staphylococcic infections we have recorded 11 recoveries from staphylococcic meningitis treated with bacteriophage, of which 7 are considered to be entirely acceptable as recoveries from diffuse cerebrospinal staphylococcic leptomeningitis. Two of the patients, H. D. and W. R., have already been reported on in medical literature.

One patient who apparently recovered from diffuse meningitis subsequently died after unsuccessful craniotomy for an abscess of the brain, and her case is therefore omitted from the group of valid instances of recovery.

A case of local cerebral meningitis and one of local cervical pachymeningitis, with recovery, are also kept separate from the group of cases of diffuse meningitis. Finally 1 case is considered unacceptable because of inadequate evidence.

Recovery from staphylococcic meningitis may be achieved by the skilful use of bacteriophage without accessory therapy. However, this disease is in any case very dangerous, and we recommend the use of a sulfonamide drug, especially sulfathiazole or sulfapyridine, along with bacteriophage. Antitoxic serum may also be added to this therapeutic combination during the first week.

Bacteriophage therapy should be continued long after apparent clinical recovery, in order to prevent the development of dangerous sequelae, especially abscess of the brain.

MEDIASTINAL EMPHYSEMA AND BILATERAL SIMULTANEOUS PNEUMOTHORAX COMPLICATING TRACHEOTOMY IN AN ADULT

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The presence of air within body tissues has been described for many years, and the causes of such a condition are varied. Emphysema, regardless of the tissues affected, may be absorbed without complication; on the other hand, serious consequences may develop, even to the point of endangering life. Subcutaneous emphysema usually clears in the course of a few hours or a few days and the patient is no worse for the experience, while emphysema of the deeper body tissues, especially those of the mediastinum, may lead to graver complications, such as pneumothorax, either unilateral or bilateral, or to complete or partial circulatory collapse. The extent of the dissemination of air through body tissues is governed by the mechanical forces at work and by the anatomic, physiologic or pathologic state of the tissues. Thus, small amounts of air injected directly beneath the surface of the skin will remain localized, but if the pressure is raised and more air injected, more widespread spaces will be opened in the tissues and the air will diffuse over greater areas. It is well known that if the eustachian tube catheter is misplaced submucosally in or about the fossa of Rosenmüller, air blown under pressure will make its appearance in the cervical region at the angle of the mandible, and that if the air continues to be blown with enough force it will spread down the tissues of the neck even to the clavicle.

TYPES OF EMPHYSEMA

Emphysema may be described as subcutaneous, retroperitoneal, interstitial, periarterial, perivenous, perirenal or mediastinal. Such terms as pneumopericardium and pneumomediastinum are also used.

Emphysema may be classified according to the various conditions causing it. Such classifications are for the most part merely descriptive, in the sense that a clue is given as to the source of introduction of air.

Traumatic lesions, either of the crushing or of the incision type, may be associated with emphysema. Early in the nineteenth century Morgan [1] noted that subcutaneous emphysema of the forehead developed

1. Morgan: Fracture of the Os Frontis into the Frontal Sinus, with Extravasation of Air into the Cellular Membrane of the Eyelids, Lancet **10**:31, 1826.

in a boy after an injury to this area immediately after he blew his nose. Newman [2] reported widespread subcutaneous emphysema following traumatic rupture of the stomach. Bishoff [3] employed multiple cutaneous incisions in treating a patient with widespread subcutaneous emphysema that followed a crushing injury to the thorax by a cartwheel. He stated that the air rushed out of the tissues so rapidly that it "blew out the flame of a wax light." Traumatic rupture of the esophagus by a questionable foreign body was followed, according to Pearce,[4] by widespread subcutaneous and mediastinal emphysema and bilateral pleural effusions. During World War I, Hayward [5] reported that widespread subcutaneous emphysema of the trunk and chest and perforation of a lung developed in a soldier after injury to the buttock by a bayonet. Since the advent of peroral endoscopy, traumatic rupture of the esophagus followed by subcutaneous and mediastinal emphysema has become a well known clinical entity.

Childbirth may be complicated by subcutaneous emphysema of the supraclavicular spaces, the neck and the face. Such cases have been reported by Klots,[6] Milne [7] and Murray.[8]

Emphysema may also occur in association with diseases of the chest. In 1918-1919, during the widespread epidemic of influenza, Symmers [9] and Berkley and Coffen [10] demonstrated cases complicated by subcutaneous emphysema, mediastinal emphysema and spontaneous pneumothorax. In the same epidemic Kelman [11] also found air in the interstitial tissues of the lungs and within the mediastinum at post-

2. Newman, A. J.: A Case of General Emphysema Following Rupture of the Stomach: Double Intussusception of the Ileum, Lancet **2**:728, 1868.

3. Bishoff: Rapid and Extensive Emphysema with Severe Collapse, from Passage of Cartwheel over the Thorax, Treated at Once with Marked Relief by Multiple Punctures of the Skin: Rapid Convalescence, Brit. M. J. **1**:163, 1884.

4. Pearce, W. H.: An Unusual Case of Emphysema: Necropsy; Remarks, Lancet **2**:1221, 1886.

5. Hayward, J. D.: Bayonet Wound of Buttock: Lung Punctured; Surgical Emphysema, Lancet **2**:199, 1917.

6. Klots, cited by Graham, E. A.; Singer, J. J., and Ballon, H. C.: Surgical Diseases of the Chest, Philadelphia, Lea & Febiger, 1935, p. 198.

7. Milne, G.: Subcutaneous Emphysema During Labour, Brit. M. J. **1**:262, 1917.

8. Murray, J.: "Surgical" Emphysema During Parturition, Brit. M. J. **1**:14, 1917.

9. Symmers, D.: Pathologic Similarity Between Pneumonia of Bubonic Plague and of Pandemic Influenza, J. A. M. A. **71**:1482 (Oct. 12) 1918.

10. Berkley, H. K., and Coffen, T. H.: Generalized Interstitial Emphysema and Spontaneous Pneumothorax as Complications of Bronchopneumonia, J. A. M. A. **72**:535 (Feb. 22) 1919.

11. Kelman, S. R.: Experimental Emphysema, Arch. Int. Med. **24**:332 (Sept.) 1919.

mortem examination in persons who had died of the disease. Boehme [12] has reported subcutaneous and mediastinal emphysema following a coughing attack during the course of pneumonia in an infant. Neffson and Bullowa [13] stated that subcutaneous emphysema and bilateral pneumothorax were complications in a patient 2 years old who required tracheotomy during the course of influenza. Dolgopol and Stern [14] reported a case of diphtheria complicated with subcutaneous emphysema in a child 2½ years old, while Graebner [15] described pneumomediastinum and pneumopericardium developing in children with obstructive laryngitis.

Foreign bodies (corn) in the lungs were reported by Welchel [16] to have caused subcutaneous emphysema of the face, lateral part of the thorax and upper portion of the body in a child 2 years old.

In 1938 Hamman [17] reported 7 cases of spontaneous idiopathic mediastinal emphysema and spontaneous pneumothorax diagnosed by clinical findings. None of the patients had any apparent disease within the chest, and all of them recovered, even though 2 had associated pneumothorax. Morey and Sosman [18] have also reported a case of idiopathic mediastinal emphysema and pneumothorax.

Surgical emphysema may be encountered in various and widespread areas of the body. In 1860 Erichsen [19] and Tatum [20] independently reported cases of widespread subcutaneous emphysema following puncture of the urinary bladder through the rectum for retention. Medias-

12. Boehme, G. F.: A Case of True Mediastinal Emphysema, M. Rec. **95**:1052, 1919.

13. Neffson, A. H., and Bullowa, J. G. M.: Influenza with Simultaneous Bilateral Spontaneous Pneumothorax and Subcutaneous Emphysema: Report of a Case, with Comment on Mechanism of Production, Arch. Otolaryng. **28**:388 (Sept.) 1938.

14. Dolgopol, V. B., and Stern, M. D.: Interstitial Emphysema of the Lung with Spontaneous Pneumothorax and Subcutaneous Emphysema: Demonstration of Air in the Septums of a Human Lung, Arch. Otolaryng. **31**:141 (March) 1940.

15. Graebner, H.: Pneumopericardium and Pneumomediastinum in Cases of Acute Obstructive Laryngitis, Arch. Otolaryng. **29**:446 (March) 1939.

16. Welchel, H. C.: Subcutaneous Emphysema in a Child: Cause; Foreign Body in the Bronchi; Case Report, J. M. A. Georgia **6**:249, 1917.

17. Hamman, L.: Spontaneous Mediastinal Emphysema, Bull. Johns Hopkins Hosp. **64**:1, 1939.

18. Morey, J. B., and Sosman, M. C.: Spontaneous Mediastinal Emphysema, with Report of a Case Associated with Spontaneous Pneumothorax, Radiology **32**:19, 1939.

19. Erichsen: Perineal Emphysema, Spreading to Upper Parts of the Body, from Puncture of the Bladder Through the Rectum, for Retention, Lancet **1**:89, 1860.

20. Tatum: Perineal Emphysema, Spreading to the Upper Parts of the Body, Lancet **1**:90, 1860.

tinal emphysema was noted by Parfitt and Crombie [21] following therapeutic pneumothorax for pulmonary tuberculosis. Banyai and Jergens [22] diagnosed a like condition following therapeutic pneumoperitoneum in a patient in whom pneumothorax also developed. After operating on 2 patients for carcinoma of the esophagus, Faure [23] reported that both died. Both had large drains in the posterior portion of the mediastinum, and he believed that enough air was sucked in about the drains to cause "extrapleural pneumothorax" of such severe degree that slow suffocation ensued.

Alexander and Follet [24] stated that an area of subcutaneous emphysema 4 inches (10 cm.) wide developed around an appendectomy wound after the patient coughed and that the air was absorbed without difficulty.

Van Bokay [25] found that mediastinal emphysema developed 4 times in a series of 2,000 intubations in children.

Although he did not report the case until 1918, Buford [26] stated that in 1898, while he was helping Dr. Fenger with a cervical gland dissection, the patient became deeply cyanotic and collapsed. This accident was attributed to air's being sucked into the mediastinum. Buford [26] had the same experience in 1916 with a patient of his own during thyroidectomy. Gold [27] confirmed this observation and added that mediastinal emphysema is a typical complication of substernal strumectomy and that collections of air which remain in the mediastinum can be demonstrated for some time. He further expressed the opinion that it is not uncommon to find blood staining the entire mediastinum after operations on the neck. Mediastinal emphysema and associated bilateral pneumothorax following thyroidectomy were reported by Keis.[28] Barrie [29] performed autopsies on 3 adult patients who died within twenty-four hours after thyroidectomy, finding mediastinal emphysema and

21. Parfitt, C. D., and Crombie, D. W.: Five Years' Experience with Artificial Pneumothorax, Am. Rev. Tuberc. **3**:385, 1919.

22. Banyai, A. L., and Jergens, G. H.: Accidental Pneumothorax During Pneumoperitoneum Treatment, Am. Rev. Tuberc. **42**:688, 1940.

23. Faure, J. D.: The Surgery of the Posterior Mediastinum: Its Past and Its Future, Bull. Johns Hopkins Hosp. **16**:125, 1905.

24. Alexander, M. E., and Follet, E. C.: Subcutaneous Emphysema, with the Report of Several Cases, Particularly One with Very Extensive Generalized Emphysema, J. A. M. A. **72**:930 (March 29) 1919.

25. Van Bokay, cited by Graham, E. A.; Singer, J. J., and Ballon, H. C.: Surgical Diseases of the Chest, Philadelphia, Lea & Febiger, 1935, p. 196.

26. Buford, C. G.: The Entrance of Air into the Mediastinum During Operations on the Base of the Neck, Surg., Gynec. & Obst. **26**:540, 1918.

27. Gold, cited by Graham, E. A.; Singer, J. J., and Ballon, H. C.: Surgical Diseases of the Chest, Philadelphia, Lea & Febiger, 1935, pp. 193-195.

28. Keis, cited by Barrie.[29]

29. Barrie, H. J.: Interstitial Emphysema and Pneumothorax After Operations on the Neck, Lancet **1**:996, 1940.

bilateral pneumothorax in all 3. During the operation on 1 of these patients a sucking noise was heard, and because of this the right internal jugular vein was ligated.

Fortunately, tracheotomy is more frequently complicated by subcutaneous emphysema than by mediastinal emphysema and its possible complications. In recent months the literature has dealt extensively with these complications during or following tracheotomy in children, but little has appeared regarding the same complications in adults. Barrie [29] cited a fourth case, in which autopsy revealed bilateral pneumothorax in a woman on whom a tracheotomy had been performed for edema of the larynx arising from cellulitis of the neck. No comment was made on the clinical course of this patient.

One of the earliest reports in this country of mediastinal emphysema and pneumothorax complicating tracheotomy in children was published by Iglauer [30] in 1915. While he was doing a tracheotomy on a child 23 months old the patient struggled violently and at the close of the operation was near collapse. Roentgen examination confirmed the diagnosis of pneumothorax (right side). Simpson [31] reported this complication following tracheotomy in a child with fulminating laryngotracheobronchitis. Michels [32] cited cases of mediastinal emphysema and pneumothorax in children following tracheotomy for acute laryngeal obstruction. He further emphasized that such complications in children are not as rare as they are thought to be.

MODES OF PRODUCTION OF MEDIASTINAL EMPHYSEMA AND PNEUMOTHORAX

Small amounts of air in the mediastinal tissues, introduced either through the neck by a surgical procedure or through the interstitial tissues of the lungs by disease or idiopathically, usually cause little trouble and are absorbed readily. If greater amounts of air are introduced into the mediastinum, it may become so distended that the pleura allows passage of air, causing pneumothorax, or the pressure may be so great that circulatory disturbances are threatened. Clinically, air in the mediastinum may cause pain that simulates cardiac pain. It may also produce a characteristic rub audible through the stethoscope, and it may or may not be outlined by means of roentgen rays.

Experimental studies on animals have greatly added to the knowledge concerning the modes of production of mediastinal emphysema and pneu-

30. Iglauer, S.: Accidental Pneumothorax During Tracheotomy, with Report of a Case, Ann. Otol., Rhin. & Laryng. **24**:303, 1915.

31. Simpson, W. L.: Pneumothorax Complicating Tracheotomy in Fulminating Laryngotracheobronchitis, Arch. Otolaryng. **26**:411 (Oct.) 1937.

32. Michels, M. W.: Pneumothorax and Mediastinal Emphysema Complicating Tracheotomy, Arch. Otolaryng. **29**:842 (May) 1939.

mothorax. Macklin,[33] Kelman[11] and Joannides and Tsoulos[34] have shown in experimenting with animals that if the intrapulmonic pressure is raised to a great enough degree, air will escape from the lungs into the interstitial tissues of the lungs and travel along the blood vessel sheaths to the mediastinum. They have further shown that if the intrapulmonic pressure is maintained and if enough air escapes into the mediastinum to raise the pressure there to a sufficient degree, pneumothorax will occur by leakage of air through the mediastinal pleura. Air may also be directed along the fascial spaces to the neck, to the axillas or downward in the retroperitoneal spaces as far as the kidneys. Kelman[11] demonstrated interstitial emphysema of the lungs and emphysema of the mediastinum and pericardium in rabbits after the animals were thrown into anaphylactic shock by the use of egg white and sheep serum. Macklin[33] expressed the belief that the air may escape from the lung tissues through the "alveolar bases" and that the path of the air from this point on is along the perivascular channels. Boyd[35] and Dolgopol and Stern[14] pointed out that the path that the air travels may be along the lymphatic spaces. The latter authors expressed the opinion that they could demonstrate this phenomenon microscopically in septums of the human lung and also expressed the belief that the air traveled to the periphery of the lungs and escaped to the retropleural tissue spaces by way of pleural adhesions. Berkley and Coffen[10] likewise supported the theory that air escapes into the retropleural spaces via pleural adhesions. Hamman[17] explained the occurrence of the idiopathic mediastinal emphysema in the cases that he reported by the theory that air escapes from the lungs to the interstitial tissues and travels thence to the mediastinum in the perivascular spaces. In the reports by Banyai and Jergens[22] concerning patients in whom mediastinal emphysema and pneumothorax developed during the course of therapeutic pneumoperitoneum, the opinion was expressed that enough air to produce the pneumothorax escaped into the retroperitoneal spaces and dissected its way upward to the mediastinum.

That mediastinal emphysema and pneumothorax may follow tracheotomy has been amply shown both experimentally and clinically. As early as 1886 Champneys[36] tracheotomized stillborn babies and after

33. Macklin, C. C.: Pneumothorax with Massive Collapse from Experimental Local Over-Inflation of the Lung Substance, Canad. M. A. J. **36**:414, 1937.

34. Joannides, M., and Tsoulos, G. D.: The Etiology of Interstitial and Mediastinal Emphysema, Arch. Surg. **21**:333 (Aug.) 1930.

35. Boyd, W.: A Text-Book of Pathology, ed. 2, Philadelphia, Lea & Febiger, 1934, p. 481.

36. Champneys, F. H.: On Some Points in the Practice of Artificial Respiration in Cases of Stillbirths and of Apparent Death After Tracheotomy, Am. J. M. Sc. **91**:445, 1886; cited by Iglauer.[30]

administering artificial respiration found that mediastinal emphysema as well as pneumothorax developed in some of them. He further pointed out: "If the entrance of air into the trachea be interfered with during forcible inspiratory efforts, and if at the same time the deep cervical fascia be opened as a preliminary to tracheotomy, then a potential passage into the thorax becomes established, and it is through this passage that the air penetrates the mediastinum. If the pressure is equalized, it goes no further; but if the pressure is not equalized it tends to burst the mediastinum and distend the pleural sac." Michels [32] expressed the opinion that mediastinal emphysema and pneumothorax developed in some of his patients in this manner, with the air traveling along the pretracheal fascial spaces to the mediastinum.

Ballon and Francis [37] as well as Macklin [33] demonstrated that pneumothorax could be produced by injecting air directly into the mediastinum of rabbits. The former authors also showed that when a fistula was made in the posterior surface of the trachea air dissected to the mediastinum, to the limbs, over the wall of the chest, to the retroperitoneal tissues and to the kidneys. In 1932, Hill [38] reported a rupture of the trachea in a newborn infant, causing subcutaneous emphysema of the neck. Barrie [29] injected air into the mediastinum of cadavers and produced pneumothorax even with moderate pressures.

Clinically, one must not overlook the importance of a patient's struggling and fighting for air against the closure or partial closure of the glottis coincident with the opening of the deep cervical fascial spaces during tracheotomy. The violent respiratory efforts in such cases bring into action all the accessory muscles of respiration, and since little or no air is being moved in and out of the lungs, enough negative pressure is created within the thoracic cage literally to "pump" air in and out of the mediastinum through the tracheotomy wound. In the adult patient whose case is to be reported here, air mixed with blood was sucked into and forced out of the lower portion of the tracheotomy wound with each respiratory effort. This continued as long as the patient was not moving air through the closed glottis and ceased when the trachea was opened.

In children, as is well known, the high anatomic position of the pleural domes may subject these structures to direct injury during tracheotomy. On the other hand, such direct injury to the pleura in adults must be exceedingly rare.

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37. Ballon, H. C., and Francis, B. F.: Consequences of Variations in Mediastinal Pressure: Mediastinal and Subcutaneous Emphysema, Arch. Surg. **19**:1627 (Dec., pt. 2) 1929.

38. Hill, F. T.: Three Unusual Endoscopic Cases Occurring Consecutively, Ann. Otol., Rhin. & Laryng. **41**:94, 1932.

Richards [39] has reported his belief that the pneumothorax which occurred in cases of acute laryngotracheobronchitis was due to direct rupture of the visceral pleura, even though tracheotomy had been performed and no tear in the lung surface could be demonstrated.

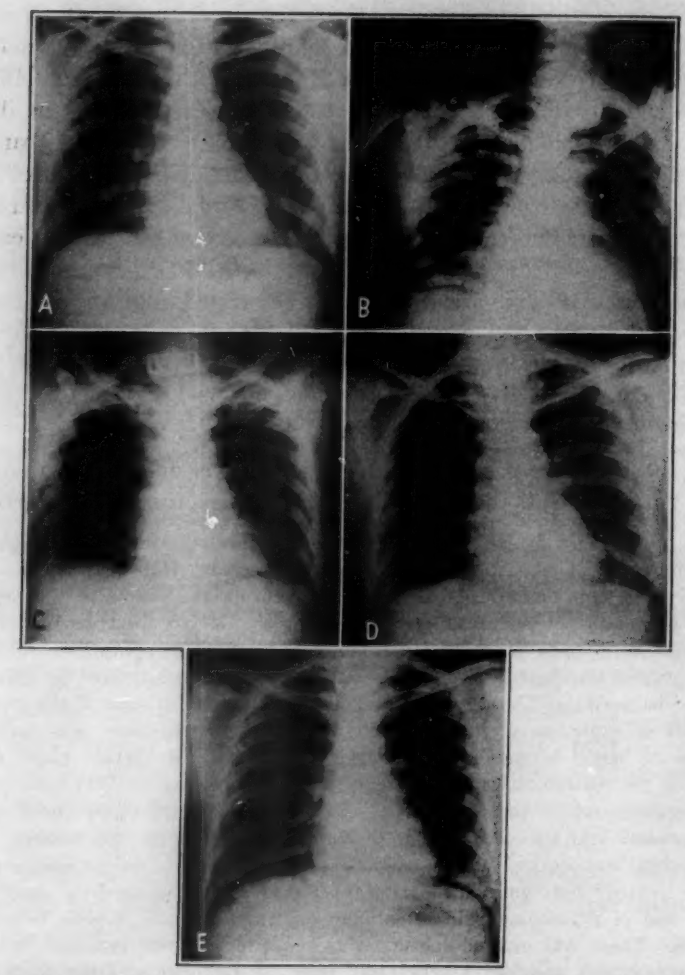
That mediastinal emphysema affects the circulation has been shown experimentally in rabbits by Ballon and Francis.[37] They found that when a balloon was placed in the anterior mediastinum of these animals and distended with air, a compression of the great veins of the thorax and a fall in blood pressure were noted. In addition, Joannides and Tsuolos [34] found that when they overdistended the lungs of dogs, producing the changes under discussion, air embolism developed in 80 per cent of their subjects. Clinically, the effect of mediastinal emphysema on the circulation may be of alarming proportions, especially if pneumothorax is also present. Buford [26] stated that in his case of mediastinal emphysema complicating thyroidectomy, venesection cured the patient by relieving the circulatory distress.

REPORT OF A CASE

In the following case mediastinal emphysema and bilateral simultaneous partial pneumothorax occurred in a woman during tracheotomy.

Mrs. O. C., aged 35, had a right hemilaryngectomy performed in the University of Michigan Hospital, Aug. 17, 1940, for carcinoma. Her convalescence from this operation was uneventful. Several times during the course of the next few weeks granulation tissue was removed from the larynx because of laryngeal obstruction, and these procedures were unattended with complications. Roentgen examination of the chest carried out on October 21 (*A* in fig.) showed the pulmonary fields to be normal. The laryngeal obstruction continued in spite of the numerous removals of granulation tissue, and on October 28 tracheotomy was performed. Because of keloid formation and a large adenoma of the thyroid gland directly overlying the trachea, difficulty was experienced in locating it. The patient began to struggle violently for air, and air bubbles mixed with blood could be seen being sucked into the deep tissues of the lower portion of the wound. When the trachea was opened and a cannula placed within it, the patient's struggle for air ceased; but immediately after operation she complained of shortness of breath and of a stabbing pain radiating from front to back directly beneath the sternum. There was marked subcutaneous emphysema of the face and neck. She appeared cyanotic and had a very rapid pulse. Examination of the chest at this time showed hyperresonance and absence of breath sounds and hyperresonance in both upper pulmonary fields. In addition, the hyperresonance extended over the whole mediastinum, and the heart sounds, although not shifted to the right or left, were distant. A tentative diagnosis of bilateral simultaneous spontaneuos pneumothorax was made and roentgenograms of the chest were made with portable apparatus. As *B* in the figure shows, there was a partial collapse of each lung with no shift of the mediastinal structures. Nine hundred cubic centimeters and 600 cc. of air were withdrawn from the left and the right pleural cavity respectively

39. Richards, L.: A Further Study of the Pathology of Acute Laryngotracheobronchitis in Children, Ann. Otol., Rhin. & Laryng. **47**:326, 1938.



A, normal chest; stereoscopic roentgenogram taken one week before tracheotomy. *B*, roentgenogram taken with portable apparatus immediately after tracheotomy. Unfortunately the patient was slightly rotated. Both pleural spaces contain air and subcutaneous emphysema is pronounced. Note the fuzziness and broadening of the mediastinum. *C*, roentgenogram taken with portable apparatus three days after tracheotomy. Both lungs are completely reexpanded, yet there is still a broadening of the mediastinum as well as subcutaneous emphysema. *D*, one of stereoscopic roentgenograms of the chest taken seven days after tracheotomy. Subcutaneous emphysema is still present. Both lungs are expanded, and there is narrowing of the mediastinum toward normal. *E*, one of stereoscopic roentgenograms of the chest taken fifty days after tracheotomy, showing an apparently healthy condition. Note the tracheotomy tube still in place.

by the use of the therapeutic pneumothorax apparatus. The pain beneath the sternum disappeared immediately, the cyanosis decreased, the patient's breathing became easier and the pulse turned toward normal.

The patient's course from here on was uneventful. At the time of tracheotomy, in order to help seal off the mediastinum from further entrance of air, the lower portion of the tracheotomy wound was packed with gauze, which was removed at the end of forty-eight hours.

Roentgenograms taken three days later with portable apparatus (*C* in fig.) showed the lungs to be completely reexpanded and the subcutaneous emphysema less. Seven days postoperatively the patient was able to go to the x-ray department for posterior-anterior stereoscopic roentgenograms of the chest. As may be noted from *D* in the figure, the chest appeared to be normal, but there was still some subcutaneous emphysema in the supraclavicular areas. Although the tracheotomy tube has remained in place, the patient's health to the time of writing has been excellent. A recent roentgenogram (*E* in fig.) shows the chest to be normal.

COMMENT

No doubt if a bronchoscope had been placed in this patient's trachea before tracheotomy was started, the complications would have been prevented, for in this manner the violent struggling of the patient to draw air into the lungs against a closed glottis would have been avoided. It is possible that the air would have been absorbed from the pleural spaces without being removed mechanically. However, in view of the distention of the mediastinum by air, plus the added factor of bilateral spontaneous partial pneumothorax, it was deemed imperative to relieve the patient's obvious respiratory as well as her circulatory distress. The relief the patient experienced after the withdrawal of air from both pleural spaces was dramatic and permanent.

CONCLUSIONS

The types of emphysema are discussed, with special emphasis on their causation.

The modes of production of mediastinal emphysema and pneumothorax are discussed. The various paths that the air may follow, either by overdistending the lung or by introducing air directly into the mediastinum, are pointed out.

The fact that the effect of mediastinal emphysema on the circulatory system cannot be overlooked is emphasized.

The case of an adult with mediastinal emphysema and bilateral simultaneous partial pneumothorax complicating tracheotomy, in which immediate aspiration of the pleural sacs was followed by recovery, is presented.

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SUBDURAL ABSCESS COMPLICATING FRONTAL SINUSITIS

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Subdural abscess complicating frontal sinusitis is an important yet little recognized entity. It is mentioned infrequently as being of pathologic interest and hardly ever is thought of as warranting clinical consideration. The numerous other conditions that often precede, accompany or follow subdural abscesses have tended to overshadow the significance of the latter and to obscure the fact that the development of a subdural abscess may be one of the most important stages in the progression of an infection which, if unchecked, is fatal.

It cannot be said that the recognition of subdural abscesses clinically will afford any revolutionary changes in present knowledge of the intracranial extension of infection from the frontal sinus or that treatment of these lesions holds great possibility of materially reducing the mortality rate. Yet it may be hoped that a better understanding of the pathologic process will serve a useful purpose in emphasizing the danger of neglected or improperly treated frontal sinusitis. It may also be hoped that the prompt recognition and treatment of a subdural abscess will sometimes save a life.

Three cases in which the presence of a subdural abscess was the most prominent complication of purulent frontal sinusitis will serve as a basis for the discussion to follow.

REPORT OF CASES

CASE 1.—Frontal sinusitis and headache were present for one month. A sudden loss of consciousness and a mild convulsion were followed by severe headache, stupor, fever and leukocytosis. There were papilledema, dilatation of the left pupil, left hemiparesis and a bilateral Babinski sign. The spinal fluid showed increased pressure, 29 leukocytes and no growth on culture. Pus was drained from the left subdural space by trephination. Death occurred two days later. Autopsy showed left frontal sinusitis with a defect in the posterior bony plate and in the dura permitting direct communication with the subdural space.

A 39 year old man was admitted to the New York Hospital on March 8, 1937, in a semistuporous state, complaining bitterly of headache.

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During an acute cold four weeks prior to admission he had suffered from frontal headache on the left side. He was treated by his physician for frontal sinusitis with frequent mild protein silver packs in the nose, which gave some relief. However, he was never completely free of headache, and two days prior to admission, while driving his car, he suddenly lost consciousness and had a short convulsive seizure, after which he was unconscious for three hours. When brought to the hospital two days later he was alternately stuporous and restlessly crying out with pain in the head.

The temperature was 39 C. (102.2 F.) (rectally), the pulse rate 75 and the blood pressure 160 systolic and 60 diastolic. He could be roused sufficiently for cooperation in the examination. High in the left nasal passage there was a purulent discharge, and the turbinates were greatly swollen on both sides. The neck was slightly stiff, and there was supraorbital tenderness on the left. The left pupil was widely dilated. Both optic fundi showed engorgement of the retinal veins and early papilledema. Motility in the lower part of the left side of the face was weak. Power in the left extremities was weak, and deep tendon reflexes on this side were sluggish. The Babinski sign was present bilaterally.

The blood leukocyte count was 28,000, with 85 per cent polymorphonuclear leukocytes, half of which were immature. A lumbar puncture disclosed spinal fluid under an initial pressure of 400 mm. of water; the cell count was 29 cells per cubic millimeter (19 polymorphonuclear leukocytes and 10 lymphocytes); the total protein content was 0.15 Gm. per hundred cubic centimeters; cultures of the fluid were sterile.

Twelve hours after admission, openings were made by trephine in each parieto-occipital region of the skull for the purpose of exploration or ventriculography if the latter was indicated. Incision of the dura on the left side released a large amount of thick odorless pus from the subdural space. The space was gently irrigated with saline solution through a tiny catheter threaded over the surface of the brain in all directions, and slips of gutta-percha were left in the space for drainage. However, there was little drainage thereafter. Cultures of the pus, as well as blood cultures, showed a pure growth of the fusiform bacillus.

Immediate improvement followed the operation and the fever subsided, but after thirty-six hours his condition again became critical with coma and rising temperature and pulse rate. He died eight hours later.

Autopsy showed the mastoids and all the paranasal sinuses normal except the left frontal sinus, which was filled with purulent material. Through the posterior bony plate of this sinus was a hole, 1 cm. in diameter, which was continuous with a smaller hole (0.5 cm.) in the dura. The cavity of the sinus was thus in direct communication with the subdural space. A small margin of bone about the defect was soft, and infected granulation tissue on the outer surface of the dura extending for 2 cm. above and lateral to the opening indicated a chronic localized epidural infection. The subdural space over the entire left cerebral hemisphere contained pus, but none had extended to the right side, and there was no pus in the subarachnoid spaces. Over the left hemisphere the leptomeninges were thickened, and a number of cortical veins over the frontal lobe were thrombosed. Elsewhere vessels were not thrombosed, and the sagittal sinus was normal. The left cerebral hemisphere was compressed, and the right lateral ventricle was moderately dilated. There was a "pressure cone" of the cerebellum at the foramen magnum.

Microscopic examination of sections from the left frontal lobe showed leptomeningitis, thrombosis of small cortical veins, moderate destruction of cortical cells and edema of the subcortical white matter.

In case 1 the sudden onset and the rapid advance of symptoms after purulent frontal sinusitis had been present for a month were the evidence that acute perforation of the dura with discharge of pus directly from the sinus into the subdural space had occurred. The defect in the posterior bony plate of the frontal sinus was in all probability the result of localized low grade osteitis. The absence of thrombophlebitis of the sagittal sinus and the limitation of pus to the subdural space over the one cerebral hemisphere further indicated the direct route of the infection from the infected sinus through the bone and the dura to the homolateral subdural space.

CASE 2.—Recurrent pansinusitis was experienced for fourteen years. An exacerbation of frontal sinusitis with osteomyelitis of the left frontal plate required radical sinusotomy. Headache, fever, stupor, papilledema and right hemiparesis developed three weeks after operation. The spinal fluid showed increased pressure, 160 leukocytes and no growth on culture. Additional operations were performed for osteitis of the posterior plate of the left frontal sinus, localized epidural abscess and extensive subdural abscess. Death occurred five days later. Autopsy showed incomplete thrombosis of the sagittal sinus and extension of a left subdural abscess to the right side.

A 36 year old man was admitted to the New York Hospital on Nov. 2, 1940, complaining of frontal headache and recent swelling over the bridge of the nose.

He had had recurring attacks of pansinusitis for fourteen years and on two occasions had undergone nasal polypectomies. For three weeks before admission there was an exacerbation of acute sinusitis with frontal headache. A tender red swelling over the bridge of the nose developed during the week prior to admission. The temperature was normal, and the blood leukocyte count was 11,000. Roentgenograms showed frontal and ethmoid sinusitis with localized osteomyelitis in the anterior plate of the left frontal sinus.

On December 6 the frontal sinuses were opened by an incision through the left brow. Localized infection of the anterior plate on the left was found and removed. Purulent material filled both the frontal and the ethmoid sinuses. The septum between the frontal sinuses was broken through, and the ethmoid cells were curetted. The posterior plate of the frontal sinus gave no evidence of infection on inspection and was not removed. The wound was drained. Cultures of the pus showed Staphylococcus albus, Staphylococcus aureus and a growth of a nonhemolytic streptococcus.

For fourteen days the patient did well. He had persistent mild frontal headache but was up and about the ward, the wound appeared satisfactory, and there was no fever. During the next week more severe headache developed, with moderate fever and slight leukocytosis, and he kept to his bed. During this time, the wound was reexplored, but the drainage was thought to be satisfactory, and sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) therapy was instituted. Headache increased in severity principally on the left, and lethargy progressed to stupor.

On November 28 (twenty-two days after sinusotomy) he was stuporous and irrational. The temperature was 40 C. (104 F.), the pulse rate 80 and the blood leukocyte count 15,500. There were low grade papilledema, slight dilatation of the left pupil and slight but definite right hemiparesis. A lumbar puncture showed a spinal fluid pressure of 280 mm. of water. The spinal fluid contained 160 leukocytes per cubic millimeter (75 per cent polymorphonuclear leukocytes) and 0.10

Gm. total protein per hundred cubic centimeters. A culture was sterile. On the same day an exploratory trephination was made in the left frontotemporal region with the expectation of finding a subdural abscess or an abscess of the frontal lobe, but neither was encountered. The former was later shown to be present but was not evident with this exposure because the pus, not yet under excessive pressure, gravitated to more dependent regions. Exploration through the original sinusotomy disclosed a small localized area of softening of the posterior plate of the left frontal sinus. Beneath this bone was an epidural abscess with thick pus amounting to 10 cc. and limited to an area about 4 cm. in diameter. The dura was covered with granulation tissue, and since there was no evidence of perforation, the dura was not opened for fear of contaminating the subdural space.

There was no improvement after this operation, and twenty-four hours later an additional exploratory trephination showed an extensive subdural abscess on the left. From the pus nonhemolytic Staph. albus and Staph. aureus were cultured. Numerous openinngs were made in the skull on the left side, through which the subdural space was irrigated and gutta-percha drains were placed. Although the patient lived for five days more, there was never any sign of improvement, and he died in coma with high fever. During this period, he continued to receive sulfathiazole, the blood cultures were sterile and daily lumbar punctures showed sterile cerebrospinal fluid with less than 100 leukocytes per cubic millimeter. The cerebrospinal fluid pressure averaged 250 mm. of water, and the brain herniated through the cranial openings, preventing any further drainage of the subdural space.

At autopsy little infection was found in the bone about the margins of the openings in the anterior and posterior plates of the frontal sinus. Pockets of pus were present in the subdural space over the left hemisphere, and the pus had extended under the falx to the subdural space over the right hemisphere. No pus was found in the subarachnoid space. The surface of the right hemisphere was not remarkable in appearance except for some flattening of the convolutions, but the left showed areas, particularly in the frontal lobe, of softening and venous thrombosis. Many of the more anterior superior cerebral veins on the left were thrombosed, and the anterior extent of the sagittal sinus for a distance of 4 cm. was partially occluded with the thrombus.

Microscopic examination of sections through the brain showed a moderate leptomeningeal reaction and cortical hyperemia on the right. On the left there were cortical necrosis, particularly in the frontal lobe, venous thrombosis, petechial hemorrhages and marked hyperemia in both the gray and the white matter.

The sequence of events in case 2 serves to emphasize some of the important aspects of the disease under discussion. Removal of the diseased anterior plate and open drainage of the frontal sinus in cases such as this constitute a standard and, as a rule, satisfactory procedure. The surgeon in this case found the posterior bony plate of the sinus intact at the first operation and again when the sinus was explored two and a half weeks later. In keeping with common practice the posterior plate was therefore not opened, yet subsequent findings demonstrated that a small area of localized osteitis was present as well as an epidural abscess.

When the exploratory trephination was made in the frontotemporal region, it was done with the expectation of finding a subdural abscess.

The failure to demonstrate the abscess which was undoubtedly present was due to the gravitation of the pus to dependent regions of the subdural space. The opening should have been made in a dependent region or the head should have been turned after the dura was opened. By the time the exploration was repeated, twenty-four hours later, the pus in the subdural space had increased greatly in amount and the dura was under tension.

Thus, the delay in recognizing and draining first the epidural abscess behind the infected bony plate of the frontal sinus and next the subdural abscess in its early stage of development allowed this infection to spread irremediably.

CASE 3.—Frontal sinusitis and frontal headache on the left existed for one month. Increased headache and chills were followed in twenty-four hours by drowsiness, aphasia and right hemiparesis. The spinal fluid was under increased pressure, contained 300 leukocytes and was sterile on culture. A subdural abscess covering the left cerebral hemisphere and an epidural abscess behind the left frontal sinus were drained. Death occurred four days later. Autopsy showed purulent frontal and ethmoid sinusitis with extension of infection through the posterior plate of the left frontal sinus to the epidural and subdural spaces.

A 21 year old man was admitted to the New York Hospital on April 19, 1941, complaining of headache, fever and chills.

During the preceding month he had been under treatment for sinusitis without much improvement. Frontal headache, principally on the left, had been a persistent symptom, but twenty-four hours prior to admission this headache became much worse and extended to involve the entire left side of the head and the suboccipital region. Further, several short chills had occurred, followed by fever, and he had vomited several times.

The oral temperature was 38.6 C. (101.5 F.) and the pulse rate 74. There was tenderness over the left frontal sinus, with engorgement of the turbinates and marked purulent discharge from both middle meatuses. There was no stiff neck. There were no abnormal neurologic signs.

Twelve hours after admission he became drowsy and partially aphasic. During an additional twelve hours there developed facial palsy on the right and abnormal reflexes on the right side of the body. The blood leukocyte count was 26,000 with 90 per cent polymorphonuclear leukocytes, half of which were immature. A lumbar puncture disclosed spinal fluid with an initial pressure of 260 mm. of water. There were 300 leukocytes per cubic millimeter in the fluid, but the cultures were sterile. Roentgenograms showed signs only of frontal sinusitis.

On April 20 an exploratory trephination was made in the left frontotemporal region just behind the outer angle of the brow. The dura appeared normal, but when it was incised there was released from the subdural space 100 cc. of thin yellow pus. The brain was at first lax and lay 2 cm. away from the dura. The head was turned to afford optimum drainage through the opening, and the patient was asked to cough. An additional 50 cc. of pus was obtained in this manner. The subdural space was gently irrigated with saline solution, and thin gutta-percha wicks were inserted for drainage.

Then the left frontal sinus was opened through an incision in the brow. Thick pus was evacuated from both frontal sinuses and from the anterior ethmoid cells. A perforation was made in the posterior plate of the left frontal sinus though there

was no evidence of infection in the bone. An epidural collection of about 5 cc. of thick pus lay behind the bony plate, and there was granulation tissue on the surface of the dura, indicating that the infection had been present for at least several days. There was no gross perforation of the dura, but incision through this membrane disclosed pus free in the subdural space over the anterior pole of the brain. The shaggy appearance of the pia-arachnoid and the discoloration of the cortex in a small area just behind the epidural abscess suggested the likelihood of direct extension of the infection through the dura. Thin gutta-percha wicks were inserted as drains.

Cultures of the pus showed nonhemolytic Streptococcus, alpha prime. Treatment with sulfonamide compounds was initiated immediately after operation.

There was only slight, temporary improvement after operation. Drainage from the wounds was slight, and the brain soon started to herniate. The right hemiparesis and the aphasia increased, the stupor became deeper, the temperature rose to 40.6 C. (105 F.), and death occurred on the fourth day after operation.

Lumbar puncture, performed daily after operation, consistently showed high spinal fluid pressure; there were from 100 to 300 leukocytes per cubic millimeter, and cultures were sterile. Blood cultures were also sterile.

At autopsy purulent frontal and ethmoidal sinusitis was found. The bone showed no gross evidence of infection. Small pockets of pus were present in the subdural space over the entire left cerebral hemisphere, and a small amount of pus had extended under the falx to the subdural space over the right frontal lobe. No pus was found in the subarachnoid space. Hemorrhagic areas and a leptomeningeal reaction were present over the left frontal lobe and to a less degree over the rest of the left cerebral hemisphere and the right frontal lobe. The cerebral veins, especially on the left, were dilated, and some of the more anterior ones were thrombosed. There was no thrombosis in the sagittal or other venous sinuses. The left cerebral hemisphere was larger than the right, and the ventricular system was shifted to the right.

Microscopic examination of sections through the left side of the brain showed a leptomeningeal reaction and cortical softening in various stages of advancement. Some cortical veins and even small pial arteries were thrombosed. The same appearance but of less degree was present in sections from the right side.

Case 3 also demonstrates that in the presence of purulent frontal sinusitis an epidural abscess may develop without the occurrence of frank infection in the bone. There are several routes by which infection may spread from the frontal sinus to the subdural space, and it is often not possible to establish an advance by one route to the exclusion of others. But in this case the appearance at operation of the pia-arachnoid and the cerebral cortex immediately beneath the chronic epidural abscess and the absence at autopsy of thrombophlebitis of the sagittal sinus point strongly to spread of the infection directly through the dura.

COMMENT

In view of the attention directed in recent years to hematomas in the subdural space it is surprising that the subject of abscesses occupying this space has been so utterly neglected, although, aside from their common anatomic location, the two lesions bear little relation to

each other. Abscesses develop in the subdural space by direct traumatic implantation of infection or by extension from an adjacent infected site. An example of the latter which readily comes to mind is the formation of a subdural abscess, usually localized, following extension of infection from the middle ear and mastoid process. But a subdural abscess resulting from extension of infection from the frontal sinus is unmentioned in most treatises and textbooks dealing with either nasal sinus disease or intracranial infections.

Courville and Rosenvold [1] in a study of the protocols of 15,800 autopsies found 43 cases in which intracranial infection had its origin in the nasal sinuses. Among these were 8 instances of subdural infection, and in 5 or 6 of the latter the subdural involvement was secondary to empyema of the frontal sinus. Among 91 cases of intracranial rhinogenic infections, Dreyfuss [2] encountered 5 in which a subdural abscess had developed. Among 110 collected cases Gerber [3] found 9 with subdural abscess originating from frontal sinusitis. McKenzie [4] in a study of 45 cases of osteomyelitis of the skull arising from frontal sinusitis reported 3 with subdural abscess.

Anatomy.—The cranial subdural space, bounded on one side by the dura mater and on the other by the arachnoid, is a potential space just as the pleural and pericardial cavities are potential spaces. The interior of the skull is lined by the dura, the inner surface of which is comprised of flattened mesothelium similar to that found on serous membranes. It is from this cell layer that the neomembrane forms which encapsulates chronic hematomas in the subdural space and would doubtless encapsulate pus too if this was present long enough. Four processes of the dura project into the cavity of the skull; the falx cerebri, the tentorium cerebelli, the falx cerebelli and the diaphragma sellae. The arachnoid, also lined by mesothelium, invests the brain loosely, spans the sulci between the gyri and is separated from the pia mater by the subarachnoid cavity, which contains the cerebrospinal fluid.

The cranial subdural space is traversed by numerous structures sometimes referred to as "anchoring structures of the brain," namely, the cranial nerves, the infundibulum, the carotid and meningeal arteries and the numerous veins of the brain which pass from its surface to various dural sinuses. The "anchoring structures" wherever they exist tend

1. Courville, C. B., and Rosenvold, L. K.: Intracranial Complications of Infections of Nasal Cavities and Accessory Sinuses: A Survey of Lesions Observed in a Series of Fifteen Thousand Autopsies, Arch. Otolaryng. **27**:692-731 (June) 1938.

2. Dreyfuss, R.: Rhinogene Gehirnaffektionen, Internat. Zentralbl. f. Ohrenh. **6**:103, 1907.

3. Gerber, P. H., cited by Courville and Rosenvold.[1]

4. McKenzie, D.: Diffuse Osteomyelitis from Nasal Sinus Suppuration, J. Laryng. **28**:6, 79 and 129, 1913.

to hold the dura and the arachnoid in approximation, and thus at the base, at the vertex and in the longitudinal fissure, where these structures are most numerous, the subdural space is a space in name only. It is over the dorsolateral surfaces of the cerebral hemispheres, where no anatomic structures traverse the space, that large amounts of cerebrospinal fluid, blood or exudate may collect between the dura and the arachnoid.

Fluid that collects in the subdural space over one cerebral hemisphere tends to remain limited to one side of the head, but under pressure the fluid crosses to the opposite side largely via the subdural space in the longitudinal fissure, i. e., under the falx cerebri. The subdural space over the cerebellum appears to be even more remotely isolated, and rarely does subdural fluid extend beyond the tentorium cerebelli.

Pathogenesis.—While there may be variations in the extension of infection from the frontal sinus to the subdural space, the pathway is more or less direct, through the posterior wall of the sinus. Schematic representations of possible pathways of infection from nasal sinuses and extracranial foci to intracranial structures have been presented by Turner and Reynolds,[5] by Kramer[6] and by Courville and Blomquist.[7] Theoretically, infection from the frontal sinus might reach the subdural space by devious routes, and since the track of infection is often lost in a multiplicity of findings at autopsy, there may be justification for uncertainty in some cases. However, osteitis of the posterior wall of the sinus has been present in some degree in the majority of cases, and this provides the clue to the pathway of the extension.

As a result of the widespread interest shown in the problem of osteomyelitis of the skull secondary to frontal sinusitis,[8] it has been

5. Turner, A. L., and Reynolds, F. E.: Intracranial Pyogenic Diseases: A Pathological and Clinical Study of the Pathways of Infection from the Face, the Nasal and Paranasal Air Cavities, Edinburgh, Oliver & Boyd, 1931.

6. Kramer, R.: Symposium on Bacterial Meningitis: Pathways of Infection from the Paranasal Sinuses, Laryngoscope **47**:304-305 (May) 1937.

7. Courville, C. B., and Blomquist, O. A.: Traumatic Pachymeningitis Interna and Subdural Abscess, with Special Reference to Pathogenesis and Pathology, Arch. Surg. **42**:890-908 (May) 1941.

8. (*a*) Furstenberg, A. C.: Osteomyelitis of the Skull: The Ostegenetic Processes in the Repair of Cranial Defects, Ann. Otol., Rhin. & Laryng. **40**: 996-1012 (Dec.) 1931. (*b*) Williams, H. L., and Heilman, F. R.: Spreading Osteomyelitis of Frontal Bone Secondary to Disease of Frontal Sinus, with Preliminary Report as to Bacteriology and Specific Treatment, Arch. Otolaryng. **25**:196-207 (Feb.) 1937. (*c*) Behrens, H. C.: Osteomyelitis of the Skull of Otitic and Paranasal Sinus Origin, ibid. **25**:272-304 (March) 1937. (*d*) Mosher, H. P.: Osteomyelitis of the Skull: Collective Review, Internat. Abstr. Surg. **69**:417-421, 1939; in Surg., Gynec. & Obst., November 1939. (*e*) Skillern, S. R.: Osteomyelitic Invasion of the Frontal Bone Following Frontal Sinus Disease, Ann. Otol., Rhin. & Laryng. **48**:392-411 (June) 1939. (*f*) McKenzie.[4]

emphasized that the most important single factor in infection of the bone is phlebitis of the small veins which drain the mucosa of the sinus and penetrate the skull. Thrombophlebitis of the diploic veins may lead to unrestricted extension of osteomyelitis in the frontal bone, or a more circumscribed process may result only in local osteitis and focal necrosis of the posterior wall of the sinus. In either case the dura lining the skull is the next structure implicated by the advance of the infection.

The dura behind the frontal sinus presents a relatively broad exposure to infection, and the dural veins communicate both with the diploic veins and with those of the mucosa of the frontal sinus. The dura fortunately is a strong barrier to further extension of infection intracranially, and since it is not especially adherent to the skull, at least at this point, there is a tendency for infection, having reached here, to localize as an abscess between the dura and the skull. Relatively small extradural lesions with exudate varying from fibrinous to purulent collect behind localized necrotic areas in the posterior wall of the sinus, while more extensive extradural abscesses are common in cases of spreading osteomyelitis of the frontal bone. Early observers paid relatively little attention to this dural lesion, but it is known to accompany osteomyelitis of the frontal bone with such frequency that Furstenberg [8] referred to it as a feature rather than a complication. The observation has been made post mortem that occasionally phlebitis of mucosal veins of the sinus which perforate the thin bone of the posterior wall may produce exudate over the dura far in advance of change in the bones, thus indicating that dural infection is not necessarily secondary to disease in the bone. In fact, the early development of dural inflammation and an extradural abscess may induce or enhance the development of focal necrosis of bone.[8e]

The possible routes of extension of infection from the extradural to the subdural space are several. One which has been suggested [7] is an indirect route through retrograde thrombosis of the superior sagittal sinus and thence into the superior cerebral veins to infect the subdural space. It is even possible that thrombophlebitis originating in mucosal veins of the frontal sinus might extend rapidly through veins leading directly into the sagittal sinus without producing either infection of the bone or significant infection of the dura.

While there is no information regarding the frequency with which infection passes to the subdural space primarily by way of the sagittal sinus and cerebral veins, the pathologic observations in many cases indicate a more direct extension through the dura. Sometimes there apparently is extension by infiltration of successive layers of the dura, as

exemplified in case 3 and in Geraghty's [9] carefully studied case. At other times focal necrosis of the dura occurs, probably aided by the pressure of an extradural abscess. By this process an actual opening in the dura results, affording direct communication of the subdural space with the extradural abscess or with the frontal sinus if the bone has become necrotic also, as in case 1.

It is important to recognize that often a subdural abscess does not occur for some time after the development of infection in the bone and the dura. The presence of thick granulation tissue on the outer surface of the dura at the time of the development of an extradural abscess in some cases is evidence of this. Thus, the clinical recognition and prompt surgical treatment of these conditions may terminate the advance of the disease before the more serious complication of subdural abscess develops. It is also important to recognize that often the infection extends into the subdural space through the dura and that retrograde infection of the venous sinus and cerebral veins need not occur. Thus, without the complication of this initial septic thrombosis, there might be hope for recovery with prompt drainage of a subdural abscess.

It is perhaps pertinent to this discussion to mention that as a source of subdural abscess the frontal sinus is the most important of all the nasal sinuses.[10] Since frontal sinusitis is often but a part of pansinusitis or at least is accompanied by ethmoiditis, there is the question of the role of the infection in these other sinuses in the production of subdural abscess. McKenzie [4] in 1913 and others since have emphasized that as a matter of experience maxillary sinusitis is found to be the cause of osteomyelitis of the skull infrequently and ethmoidal and sphenoidal sinusitis rarely. In addition, the anatomic arrangement of the dura and the communicating veins is not conducive to the formation of extradural or subdural abscesses in sphenoidal and ethmoidal sinusitis. So, while nasal sinuses other than the frontal are commonly the source of thrombosis of venous sinuses (particularly of the cavernous sinus) and of leptomeningitis, the frontal sinus preeminently is the source of the extensive subdural abscess.

The common infecting organisms in subdural abscesses are probably the ones usually found in other intracranial infections arising from nasal sinusitis: namely, pneumococci, streptococci and staphylococci. Doubtless, the virulence of the organisms is important. The organisms found in the 3 cases reported here were respectively fusiform bacilli, streptococci and staphylococci combined, and streptococci. The first type is

9. Geraghty, W. R.: Extensive Bilateral Subdural Abscess: Microscopic Study of the Meninges and Brain; Report of a Case, Ann. Otol., Rhin. & Laryng. **45**:452-463 (June) 1936.

10. Courville, C. B.: Pathology of the Central Nervous System, Mountain View, Calif., Pacific Publishing Association, 1937.

of special interest because of the rarity of their occurrence as pyogenic organisms unmixed with others.

Pathology.—Little need be added to the observations discussed in connection with the pathogenesis of subdural abscess except to mention the evolution of the disease which, if uninterrupted, ultimately leads to overwhelming intracranial infection. The purulent exudate that collects in the subdural space as a complication of frontal sinusitis has little tendency to localize and often 100 cc. or more of pus overlies the cerebral hemisphere from pole to pole. It might even be preferable to designate the condition as empyema. Unfortunately, after surgical drainage there is a greater tendency for isolated collections to become walled off and surrounded by a neomembrane, making the problem of drainage of the entire space a difficult one. The external surface of the arachnoid and the internal surface of the dura, including sometimes the falx and the tentorium, become covered by a shaggy or velvety fibrinous exudate which should readily serve at exploratory trephination or at autopsy to distinguish the lesion from purulent leptomeningitis, with which it is likely to be confused.

The surface of the cerebrum, partly or wholly devoid of its normal markings because of the thickened arachnoid, is flattened or depressed by the pressure of the exudate. Coronal section through the cerebrum demonstrates the effects of pressure in the obliteration of the subarachnoid space, in the displacement and flattening of the homolateral ventricle and sometimes in the enlargement of the contralateral ventricle. Even when the purulent exudate has extended to the subdural space over the opposite hemisphere, the effects are greater on the initial side of the infection.

The remarkable property of the arachnoid in impeding the spread of infection to the subarachnoid space accounts for the existence of little more than a mild leptomeningeal reaction and a low degree of pleocytosis of the spinal fluid until the last stages of the disease. As a terminal event, however, septic leptomeningitis may ensue.

A common complication of subdural abscess is thrombosis of the pial vessels on the cerebral surface and of the tributary veins of the venous sinuses, particularly the superior cerebral veins. Occasionally, extension of the thrombosis in these veins results in thrombosis of the superior sagittal sinus. Venous stasis and small arterial occlusions are accompanied by edema, small cortical hemorrhages and areas of cerebral softening. If septic thrombi develop, septicemia and abscesses of the brain follow.

Symptomatology.—While many of the symptoms of acute subdural abscess are symptoms also of purulent frontal sinusitis and of other conditions complicating sinusitis, the occurrence of neurologic signs should always suggest the former. Courville [10] stated as a "clinico-

pathologic aphorism" that "in the presence of acute frontal sinusitis (empyema), the sudden onset of jacksonian convulsions, hemiplegia and (if the major side of the brain is affected) aphasia usually indicates the development of a subdural abscess."

Regarding the clinical courses of the 3 cases presented here it will be recalled that while headache, nasal discharge, fever and malaise had been present for varying periods, dramatic changes occurred in a relatively short time with the development of subdural infection. In case 1 a convulsion occurred without warning; in case 2 hemiplegia appeared after several days of increased headache and malaise, and in case 3 aphasia and hemiparesis developed twenty-four hours after increased headache, chills and vomiting.

Headache was the chief complaint of all 3 patients, and it was most severe over the frontotemporal region on the side of the abscess. Two of the patients had suboccipital headache and stiff neck. Drowsiness appears early in the illness, and while there were fluctuations in degree, there was gradual progression to stupor and coma.

Convulsions occurred in 1 of the 3 cases, but Courville [10] must have found them frequent enough to consider them of diagnostic significance. Partial paralysis of the face and of the upper and lower extremities on the contralateral side occurs both from the effects of local pressure of the abscess and from thrombosis of the cortical vessels. Occasionally, as is true with subdural hematoma, the paralysis occurs on the same side as the lesion. (See case 2.) This is the result of marked displacement of the brain causing pressure of the edge of the tentorium against the peduncle of the opposite cerebral hemisphere. In addition, there is inequality of the pupils, the larger as a rule being on the side of the lesion, but the sign is not infallible.

With regard to the laterality of the abscess it should be appreciated that although the abscess will usually be on the side of the known frontal sinusitis, other circumstances may lead to the production of an abscess on the opposite side. For example, a frontal sinus may extend across the midline, thus having its posterior wall in approximation with the dura on each side of the sagittal sinus; more often the septum between the frontal sinuses is incomplete, and both frontal sinuses are diseased though the symptoms may point largely to one. Further, if, as occasionally may happen, the subdural abscess develops by an extension of thrombophlebitis through the sagittal sinus, it is largely a matter of chance on which side the space becomes infected.

Early the optic fundi may be normal, but eventually there should develop engorgement of the veins, possibly small retinal hemorrhages and low grade papilledema.

The pulse is moderately slow and may tend toward bradycardia as intracranial pressure increases. The temperature, while elevated, is not

excessively high until the late stages of the disease. The blood leukocyte count ranges from 15,000 to 30,000, and there is a predominance of polymorphonuclear cells.

Lumbar puncture shows increased cerebrospinal fluid pressure, usually of moderate degree in the early stages but rising to 400 mm. of water or more with the increase in intracranial pressure. The fluid may be slightly xanthochromic or cloudy, and the cell count varies from a slight increase to one of several hundred with a predominance of polymorphonuclear cells. No organism can be grown on culture, and it is only in the latest stages of the disease, when septic leptomeningitis may occur, that high cell counts and positive cultures are obtained.

Roentgenograms of the skull and sinuses cannot be depended on to be of material assistance in the diagnosis of subdural abscess or even of infection of the frontal bone, which often precedes that condition. It is common experience that roentgenographic changes in the skull, like those in other bones, do not appear for about a week after infection has set in. Mosher [8d] and others have stressed that in cases of spreading osteomyelitis of the frontal bone accompanying frontal sinusitis edema of the forehead is the most useful indicator of the presence and extension of the disease. In cases of focal necrosis (osteitis) of the posterior bony wall of the frontal sinus neither edema of the scalp nor roentgenographic changes can be depended on for aid in the diagnosis of infection penetrating from the frontal sinus and impending subdural abscess.

Prevention.—A full consideration of the prevention of any of the complications of frontal sinusitis should incorporate the methods necessary to deal with frontal sinusitis properly before it spreads beyond the membranous lining of the sinus. This is the problem of the rhinologists, and though the responsibility for complications has been often assigned to them, if the principles proposed by McKenzie,[4] Mulligan and Crowe,[11] Brown,[12] Skillern,[8e] Adson and Hempstead [13] and others were followed more widely, the complications would be far fewer. There is agreement among these rhinologists that the persistence of local headache with or without fever and in spite of intensive shrinkage of the nasal mucosa and irrigation of the infected sinus calls for prompt external opening of the sinus. It has sometimes been said that external drainage of the sinus has led to spread of the infection beyond the sinus, but if the truth

11. Mulligan, E. J., and Crowe, S. J.: Treatment of Acute Infections of the Frontal Sinus, Ann. Otol., Rhin. & Laryng. **50**:499-502 (June) 1941.

12. Brown, J. M.: Frontal Sinusitis, Ann. Otol., Rhin. & Laryng. **50**:435-449 (June) 1941.

13. Adson, A. W., and Hempstead, B. E.: Osteomyelitis of Frontal Bone Resulting from Extension of Suppuration of Frontal Sinus: Surgical Treatment, Arch. Otolaryng. **25**:363-372 (April) 1937.

could be known, the extension in many cases was probably already under way by the time the operation was employed. Skillern [8e] carried the argument further in stating:

> We believe in playing safe and assuming that all acute frontal sinuses that require operation probably have some extension of the infection. We expect to find osteomyelitis, and we believe in a thorough curettage of all softened bone and hemorrhagic osteitis.
>
> We do not hesitate to expose the dura by removing the posterior plate of the sinus.

The proposal to remove the posterior bony plate as a routine in sinusotomy in all cases would probably not be justifiable, or acceptable to rhinologists. Yet the decision for removal of the posterior plate is usually based on the finding of softened bone, and that one who follows this rule may be misled and find no clue to the presence of an extradural abscess is amply demonstrated in case 2.

Thus, if the surgeon feels that there is no justification for opening the posterior bony plate at the time of providing open drainage of the sinus, he must at least be on the alert for signs of extension of the infection. Nor need he wait for the dramatic symptoms of a subdural abscess before accepting the evidence of extension. The principal point of this entire discussion would be missed if it were not stressed that in every case warning signs are present sometimes for days before the serious complication of subdural abscess occurs.

The persistence or the development of frontal headache after simple frontal sinusotomy is a strong indication of the presence of extradural infection. The dura in the region behind the sinus has been shown to be pain sensitive, and the region of reference of pain is in the local frontal region.[14] Either inflammation of the dura or pressure of a local extradural abscess is sufficient to incite pain. There may be accompanying low grade fever, leukocytosis and, in the later stages, lethargy and signs of aseptic meningitis. An unrelieved extradural abscess will almost certainly lead to a subdural abscess or another equally serious intracranial infection. Thus, the persistence of frontal pain with or without other signs calls for opening of the posterior bony plate of the sinus. Spreading osteomyelitis of the frontal bone which is almost always accompanied by an extradural abscess is not as easily overlooked as the small localized abscess, which is usually accompanied by local osteitis of the posterior plate of the sinus.

Treatment.—The treatment of a subdural abscess is primarily surgical. The measures employed should at the same time be useful in establish-

14. Ray, B. S., and Wolff, H. G.: Experimental Studies on Headache: Pain-Sensitive Structures of the Head and Their Significance in Headache, Arch. Surg. **41**:813-856 (Oct.) 1940.

ing the diagnosis. One may be reasonably certain of the diagnosis on clinical grounds alone, but it is important that in case of mistaken diagnosis the incision is not harmful in carrying infection into fields where it is not already present. It is never justifiable to open the dura deliberately in an infected field, and though the first incision in dealing with a presumed subdural abscess should be made for the thorough removal of diseased bone and the drainage of any extradural infection, the dura should be opened through a new incision in an uninfected field.

The primary incision for the identification and drainage of a subdural abscess may be made profitably in either of two places. A short vertical incision 1.5 cm. behind and just above the level of the outer angle of the brow affords the more direct approach. A burr opening is made in the skull, and the dura is incised. In the presence of a subdural abscess the dura will often be edematous, and this may be evident on the surface. Though subdural abscess complicating frontal sinusitis is usually widely spread through the space over one hemisphere, even the occasional localized abscess could be identified through this exposure or an enlargement of it. If the pus is under tension, it will well up through the incision, but in the early stages of the infection, before tension has developed, the exudate may gravitate to dependent regions, and unless the head is turned so that the dural opening lies in a dependent position, the presence of the exudate may go unrecognized, as in case 2. In the absence of positive findings further exploration with a needle for an abscess of the frontal lobe or tapping of the frontal horn of the ventricle could be carried out through this same incision.

An alternative incision may be made in the occipital region at the site commonly chosen for ventriculography. The same principles that obtain when the frontotemporal incision is employed are applicable here. The posterior incision has the disadvantage of being farther away from the source of a subdural abscess but has an advantage in case no abscess is discovered. This incision then becomes the more useful through which to carry out ventriculography if the alternative diagnosis is unlocalized abscess of the brain.

When a diffuse subdural abscess is encountered, from one to five additional openings should be made at other sites, avoiding important cortical areas. Through each opening gentle irrigation of the adjacent subdural space should be carried out with warm saline solution through a small catheter. It may even be possible to wash through from one opening to another but gentleness of manipulation is imperative. Under no circumstances should the surgeon be led into making large openings in the dura, and no attempt should be made to leave drains other than locally placed thin rubber wicks.

The initial drainage of the subdural space is usually the only one that is useful, for shortly thereafter the edematous brain seals off the space

at the openings in the dura. Thereafter, hope for recovery must be placed in the patient's ability to deal with any remaining infection or in a possible localization of intracranial infection that might lend itself to subsequent surgical drainage. Although in Gardner's [15] case the diffuse subdural abscess arose from mastoiditis, the case is in point for the exudate was drained through a single frontotemporal burr hole, and subsequently an abscess of the occipital lobe was also drained; the patient recovered. Judicious use of suitable sulfonamide compounds should increase the chances of recovery.

SUMMARY AND CONCLUSIONS

Subdural abscess is a serious, though infrequent, complication of frontal sinusitis which constitutes a distinct pathologic and clinical entity and which has not received wide recognition.

Personal experience with 3 cases serves as a basis for discussion. From these cases and a few others reported in the literature the following conclusions are drawn:

1. Acute purulent frontal sinusitis, if the sinus is not adequately drained, may result in a subdural abscess through thrombophlebitis of the small veins draining the sinal mucosa.

2. There may or may not be associated osteomyelitis of the frontal bone or local necrosis (osteitis) of the posterior bony plate of the sinus, but with rare exceptions there is some degree of inflammation of the local dura, usually with an epidural abscess, preceding the subdural abscess.

3. The extension of infection to the dura can often be recognized in ample time to prevent further intracranial complications.

4. A sudden onset of jacksonian convulsions and hemiplegia in the presence of acute frontal sinusitis usually indicates the development of a subdural abscess.

5. The subdural abscess usually is limited in the beginning to the same side as the diseased frontal sinus but tends to spread over the entire cerebral hemisphere, and in the later stages, to the opposite side.

6. Drainage of a subdural abscess should be through one or several trephine openings, preferably placed in the frontotemporal and occipital regions.

The pathologic examinations in the 3 cases reported were made in the department of pathology of Cornell University Medical College. Dr. Gervais W. McAuliffe, of the department of surgery, gave suggestions regarding the rhinologic aspects of the discussion.

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15. Gardner, W. J.: Subdural Abscess: Its Relation to Sterile Purulent Leptomeningitis, Ohio State M. J. **29**:235-238 (April) 1933.

CYST OF THE LARYNX

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In general, the occurrence of cysts in the larynx is rare. Beschorner [1] in 1877 saw 45 cysts among 693 polypoid growths. Of more than 722 benign tumors of the larynx seen at the Mayo Clinic, only 35 have been diagnosed as cysts.[2] Of these, only 3 have involved the appendix of the ventricle, like the one we are reporting. In scanning the literature, a survey reveals that the number of cysts of this type is relatively limited.

As far back as 1860, Ulrich [3] collected a number of cases in which the cysts included 50 on the vocal cords, 8 in the sinus of Morgagni and 8 in the arytenoid region. Moure,[4] in 1880, had observed 68 cases and Wolfenden [5] 165. Since that time, a great number of publications of case reports accompanied by drawings have found their way into print, and several theories about the origin of cysts have been advanced.[6]

Moure [4] gave a vivid description of a laryngeal cyst: "A tumor with clearly defined and developed wall, whose inner space has no

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1. Beschorner: Ueber Epiglottis-Cysten, Berl. klin. Wchnschr. **14**:620, 1877.

2. New, G. B., and Erich, J. B.: Benign Tumors of Larynx: Study of Seven Hundred and Twenty-Two Cases, Arch. Otolaryng. **28**:841-910 (Dec.) 1938; Tr. Sect. Laryng., Otol. & Rhin., A. M. A., 1938, pp. 17-96.

3. Ulrich, R.: Ueber Kehlkopfcysten, Würzburg, Becker, 1887.

4. Moure, E. J.: Des kystes du larynx, Rev. mens. de laryng. **1**:75, 1880.

5. Wolfenden, R. N., and Martin, S.: Studies in Pathological Anatomy, Especially in Relation to Laryngeal Neoplasms, London, J. & A. Churchill, 1888.

6. (*a*) Chamberlin, W. B.: Report of a Case of Cyst of the Larynx, Laryngoscope **27**:957-960, 1917. (*b*) Cody, C. C.: Cysts of Larynx, Texas State J. Med. **33**:581-583, 1937. (*c*) Davis, E. D. D.: Cysts of Larynx, J. Laryng. & Otol. **38**:473-476, 1923. (*d*) Klose, W.: Zwei Fälle seltener Kehlkopftumoren, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **145**:154-158, 1938. (*e*) Myerson, M. C.: Cysts of the Larynx, Arch. Otolaryng. **18**:281-290 (Sept.) 1933. (*f*) Thacker Neville, W. S.: Cyst with Displacement of Sacculus, J. Laryng. & Otol. **53**:127-128, 1938. (*g*) Woodruff, G. H.: Cyst of Epiglottis and Other Laryngeal Cysts, Illinois M. J. **66**:569-573, 1934. (*h*) Thost, A. T.: Die gutartigen Neubildungen des Kehlkopfs, in Denker, A., and Kahler, O.: Handbuch der Hals-Nasen-Ohrenheilkunde, Berlin, Julius Springer, 1929, vol. 5.

excretory duct toward the outside, neither through vessels, nor serous or mucous duct. The content is usually liquid, but is sometimes thicker, being gelatinous and colloidal in appearance. In some cases it is hemorrhagic, and is sometimes therefore confounded with an angioma."

Cysts of the larynx can be classified in two ways, according to their origin or their location. They are either acquired or congenital. The location can be, in order of frequency of occurrence, on the epiglottis, the vocal cords, the lateral wall of the larynx and finally the region of the aryepiglottic folds. Some authors have described cystic degeneration of a fibroid tumor as cyst, but this condition should be excluded from the discussion. Acquired cysts are due either to direct trauma or to inflammatory occlusion of the excretory ducts of the glands.

Traumatic cysts, according to Garré,[7] arise from transplantations of epithelium into the deeper layers by injury, a process similar to formation of an epidermoid cyst.[8] Like congenital cysts, traumatic cysts are true tumors, and similar histologic observations have been described for the two groups. The epithelium is columnar or squamous, sometimes containing goblet cells. The substantia propria possesses elastic fibers and a layer of lymph glands and lymphocytes. Though congenital cysts are usually found in the aryepiglottic fold and laryngeal wall, traumatic cysts also may occur at these locations. By far the most frequent site is the region of the epiglottis, where injury from passing food particles is more likely.

Occlusion cysts have their origin in obstruction of the excretory ducts of the glands, with subsequent stagnation of the glandular secretion.[9] These cysts in the earlier stages are lined by stratified columnar epithelium. Later, however, as a result of the increase in pressure of the fluid content, a metaplasia takes place, with a conversion of the columnar to a cuboidal or squamous epithelium. With extreme pressure the epithelium entirely disappears, so that only a fibrous wall remains. The contents of these cysts may be serous, gelatinous or even colloidal, intermixed with desquamated epithelium, small blebs of fat, and cholesterol crystals. Hemorrhagic cysts, which are also acquired, are due to extravasations of blood and lymph into the submucosal spaces with subsequent encapsulation of the mass. They, of course, have no epithelial lining.

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7. Garré, cited by Hückel, R.: Zur Kenntnis der Larynxzysten, Zentralbl. f. allg. Path. u. path. Anat. **68**:113-115, 1937.

8. Dean, W. L., and Gregg, J. B.: Implantation Cyst of Larynx, Laryngoscope **28**:74-77, 1918. Adams, W. S.: Laryngeal Dermoid Cyst, J. Laryng. & Otol. **45**:266-269, 1930.

9. Equen, M.: Retention Cyst of Larynx: Report of Case, Ann. Otol., Rhin. & Laryng. **46**:757-759, 1937.

Congenital cysts have been observed at all ages.[10] Several theories have been advanced to explain the presence of congenital cysts in the larynx. Schneider's [11] theory of displaced embryonic cells from the appendix of the ventricle seems the most acceptable and is in accordance with Kahler's.[12] Louys [13] spoke of the branchiogenic origin of the mesodermal tissue forming the cyst, while Glas [14] considered the presence of a meeting point of several germinal layers as essential for the development of a cyst. The thyroglossal origin, mostly of epiglottic cysts, was advanced by Beck,[15] but there are few facts to substantiate it. There seems to be no explanation offered for the sudden development of the anlages in later life. It is difficult to decide from the histologic observations whether an acquired or congenital formation is present. Even if one accepts all theories about the possibility of a cyst's developing in later life from an anlage, there is no definite way of establishing its origin or cause. Neither the presence of ciliated columnar epithelium nor that of glands or lymphocytes can serve as definite proof of a cyst's being congenital, as cysts resembling such cysts of the larynx are known to be found in the membranes of the nose and paranasal sinuses.

Naturally, one is inclined to assume that a cyst which shows ciliated epithelium and active glands despite pressure from its contents did not originate through the occlusion of a glandular duct but is kept growing by the inherent qualities of the cells forming its nucleus. But there is no way of ruling out the possibility that trauma, chemical or mechanical, would not elicit a tumorous growth in an area where no previous anlage

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10. (*a*) Fischer, V. E.: Congenital Cyst of Larynx, J. Pediat. **5**:491-494, 1934. (*b*) Jacobi, M., and Rascoff, H.: Cyst of the Larynx in Infancy, Am. J. Dis. Child. **49**:448-459 (Feb.) 1935. (*c*) Lorie, A. J., and Lux, P.: Congenital Cyst of the Larynx, Laryngoscope **42**:957-960, 1932. (*d*) Marx, H.: Angeborene Kehlkopfcyste, Ztschr. f. Hals-, Nasen- u. Ohrenh. **21**:376-381, 1928. (*e*) Hamilton, H. D.: Cyst of the Epiglottis, Montreal M. J. **28**:602, 1899. (*f*) New, G. B., and Erich, J. B.: Congenital Cyst of the Larynx, Arch. Otolaryng. **30**:943-949 (Dec.) 1939. (*g*) Rosenberger, H. C.: Cyst of the Larynx, and Lobus Azygos of Lung: Case Report, Laryngoscope **37**:360-366, 1927. (*h*) Snaith, L.: Congenital Cyst of the Larynx Causing Fatal Asphyxia Neonatorum, Arch. Dis. Childhood **15**:274-276, 1940. (*i*) Bellocq, G. P. (Mme.), and Pernot, R.: Étude clinique et anatomopathologique des kystes laryngés congénitaux du nouveau-né, Rev. franç. de pédiat. **9**:236-255, 1933.

11. Schneider, P.: Zur Genese der kongenitalen Larynxcysten, Ztschr. f. Ohrenh. **64-65**:358-374, 1911-1912.

12. Kahler, O.: Genese der Epiglottiszysten, Ztschr. f. Laryng., Rhin. **5**:553, 1912.

13. Louys, E.: Des kystes intralaryngés, et en particulier der kystes laryngés branchiogènes, Thesis, Geneva, Paris, F. A. Alcan, 1900.

14. Glas, E.: Ueber Larynxcysten, Arch. f. Laryng. u. Rhin. **19**:285-305, 1906-1907; cited by Thost.[6h]

15. Beck, J. C.: Cyst of Epiglottis, Laryngoscope **19**:704, 1909.

was present, in the end piece of a gland or in the appendix of the laryngeal ventricle. The size or location of a cyst cannot be regarded as indicative of its origin.

The cysts described have ranged in size from lesions the size of a pea to masses occluding the lumen of the larynx. Very large cysts have been reported by Hamilton [10e] (1899) and recently by New and Erich.[10f] All cysts of the larynx, except the hemorrhagic ones, grow slowly. Even large cysts do not give rise to severe complaints by the patient, because the air passage usually is reduced so gradually that the patient can accommodate himself without too great difficulty. Symptoms described by the patient include hoarseness, slight dyspnea, a feeling of fulness in the throat and difficulty in swallowing. Sometimes no symptoms are noted, and the cyst is discovered by accident.

The removal of these cysts is best performed by thyrotomy, which facilitates complete removal without rupture of the sac wall.

We wish to report the following case, which offers some interesting sidelights on the diagnosis of such cysts and of tumors of the larynx in general.

REPORT OF A CASE

S. G., a white man 24 years of age, came to our office with a history of slight, progressive hoarseness of about eight months' duration, accompanied by two attacks of sudden asphyxia. He had his throat "painted" a few times by the family physician without success. No further attention was given to his complaints until he was to be inducted into the army. At the induction center an obstructing tumor of the larynx was diagnosed, but the patient was declared fit for service. After some difficulty, he succeeded in obtaining deferment to have the matter adjusted.

Physical examination failed to reveal any abnormal condition. The patient was hoarse but showed no signs of dyspnea. No glands were palpable, and the outside of the neck appeared normal. Examination of the larynx revealed the left wall of the larynx to be bulging into and almost obliterating its lumen. The tumor mass was round and smooth and involved all structures from the area of the false cord to and including the base of the aryepiglottic fold. It appeared to rise from the ventricular appendix and completely involved this structure. Because of the size of the tumor, the glottis could not be seen, nor the left vocal cord, except at its posterior attachment. The movement of the left arytenoid was restricted. During phonation the tumor pressed against the structures on the opposite laryngeal wall, apparently preventing apposition of the cords. The result was a hoarse whisper. Except for a slight bulge into the left piriform sinus, no pathologic conditions were noted in this area. The mucous membrane over the tumor appeared hyperemic.

A specimen for biopsy was taken in the region of the tumor, and on this occasion palpation with an instrument gave the feeling of a semisolid mass. With a punch forceps an adequate piece of membrane was removed without major bleeding. Examination of the tissue removed revealed a highly vascular mucous membrane. The epithelium was unchanged except in the substantia, where a high state of vascularization existed. Because of the numerous thin-walled lymph channels present, the pathologist suggested the possibility that a lymphemangioma might be present.

A thyrotomy was performed with the patient under anesthesia introduced with avertin in amylene hydrate and ether. On exposure the mass was found to involve the entire left laryngeal wall, as previously noted. The left vocal cord was entirely free. As finger palpation strongly suggested a cystic tumor which

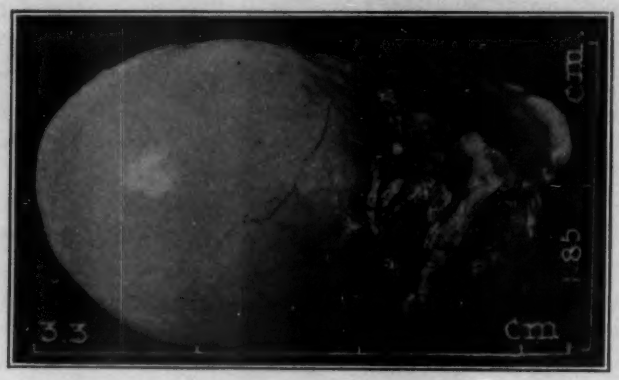


Fig. 1.—The cystic tumor.

Fig. 2.—Simple columnar ciliated epithelium lining the cyst.

might easily rupture, it was decided to separate the mucous membrane from its attachment to the thyroid by working behind the tumor rather than on the laryngeal surface. Beginning at the midline, the entire mucous membrane over the left thyroid cartilage was easily detached, releasing a greatly compressed cyst. The tumor then assumed a much larger size, and was easily peeled off from its attach-

ment to the laryngeal mucosa. By working behind the tumor, the mucous membrane of the larynx was uninjured, and the likelihood of rupturing the cyst was reduced to a minimum. The laryngeal mucosa was reattached anteriorly and the perichondrium closed over the cartilage. Tracheotomy was not necessary. Healing occurred rapidly, and the patient made an uneventful recovery. The voice was restored to normal.

The cystic tumor (fig. 1) was 3.3 cm. in length and 1.8 cm. in diameter and had a volume of 10 cc. It contained a thick, gelatinous fluid. The wall revealed a ciliated stratified columnar epithelium for the most part (fig. 2). In some areas the epithelium appeared cuboidal and cilia were absent. Numerous actively secreting goblet cells were present. The basement membrane was rather thick. In the substantia propria numerous lymphocytes were present, but no definite lymph follicles were noted.

COMMENT

Because of its location in the lateral laryngeal wall, together with the observation of stratified ciliated columnar epithelium, goblet cells and basement membrane, this cyst, according to criteria developed in the existing literature, would be classified as of congenital origin. One would generally not expect these conditions to exist in a simple glandular occlusion. However, it is best to reserve judgment until more information is obtained concerning the local influence of stagnant secretion and of trauma. It is possible that cysts like this may be similar to those encountered in the nasal and paranasal mucosa, since their structures are almost identical. The cysts of the nasal mucosa are known to arise from excretory glands and ducts. In their formation, ease of distention plays an important role, and no doubt parallel conditions exist in the formation of laryngeal cysts.

SUMMARY

Different opinions on the formation and classification of laryngeal cysts are reported.

A case is described of a cystic tumor, 3.3 cm. by 1.8 cm., and 10 cc. in fluid volume, which was removed.

It is very difficult to establish a definite diagnosis of congenital cyst in adults, since acquired and congenital cysts may offer similar manifestations.

841 East Sixty-Third Street.

CONSTRICTING DOUBLE AORTIC ARCH

REPORT OF A CASE

PETER A. HERBUT, M.D.
AND
THOMAS T. SMITH, M.D.
PHILADELPHIA

A constricting double aortic arch in infancy, although somewhat rare, occurs frequently enough to warrant the reporting of an additional case. Wolman [1] in 1939 found only 6 such cases in the literature, and to these he added 1 of his own. Schall and Johnson [2] reported 1 essentially similar in 1940, and Arana and Aguirre [3] reported a ninth case in the same year.

Wolman [1] outlined an associated symptom complex which is remarkably constant, not only in those cases reviewed by him, but in subsequent cases as well. This consists of "stridulous breathing, chronic cough, respiratory distress while feeding, failure to thrive, susceptibility to bronchopneumonia, head retraction, and malnutrition." The symptoms and course in the following case adhere closely to this pattern.

REPORT OF CASE

A white girl aged 2½ months was admitted to the service of Dr. Louis H. Clerf at Jefferson Hospital on Jan. 16, 1942, with a history of increasing respiratory difficulty. This had been present since birth, but it had recently become more evident and was now associated with severe attacks of dyspnea and cyanosis. These attacks were noted to be most severe during and after feedings.

On admission, the infant appeared to be fairly well nourished and was able to rest without noticeable respiratory distress. Physical examination revealed nothing of significance, and roentgen studies showed a normal chest with little or no increase in the breadth of the upper mediastinal shadows. The results of studies of the blood, together with other laboratory data, indicated normal conditions.

From the Department of Clinical Laboratories and Bronchoscopic Clinic, Jefferson Hospital.

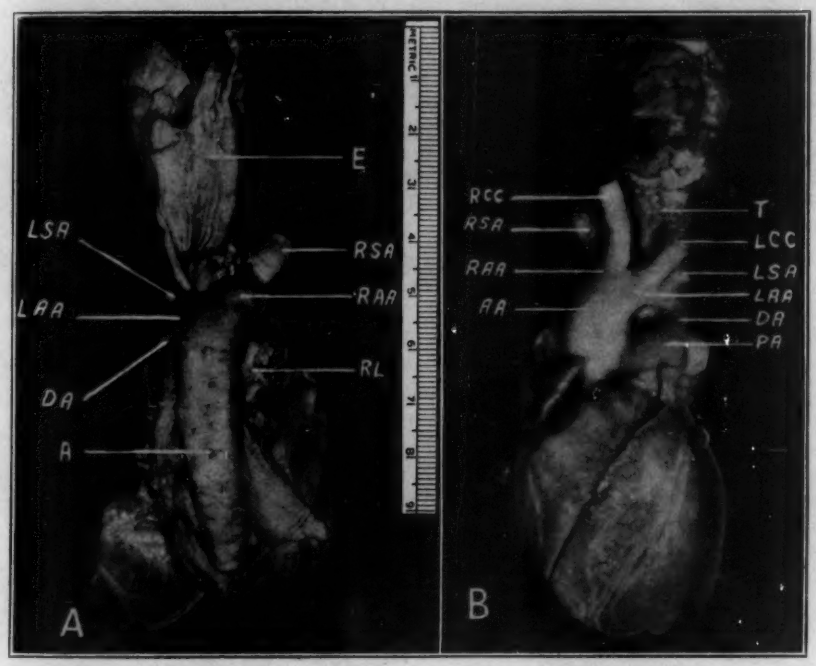
1. Wolman, I. J.: Syndrome of a Constricting Double Aortic Arch in Infancy: Report of a Case, J. Pediat. **14**:527, 1939.

2. Schall, L. A., and Johnson, L. G.: Dyspnea Due to Congenital Anomaly of Aorta, Ann. Otol., Rhin. & Laryng. **49**:1055, 1940.

3. Arana, M. R., and Aguirre, R. S.: Doble arco aórtico en un niño: su confusión con la hipertrofía del timo, Arch. argent. de pediat. **11**:331 (Oct.) 1940 (although this article was not available to us, the title suggests that it should be included in this group).

On the third day of hospitalization, the infant while feeding was seized with a severe attack of coughing and dyspnea. After this, some indrawing of the suprasternal and intercostal spaces persisted, and the respirations never again became entirely normal. The infant now lay with her head turned to the left at all times. When the head was forcibly turned to the right, breathing became more difficult and indrawing was marked. Similar severe attacks recurred with each subsequent feeding.

When the infant was placed in the Boyce position preparatory to direct laryngoscopic examination, increased respiratory difficulty was noted. When the extension of the head was increased, as was necessary for the introduction of



A, posterior view, showing the esophagus (*E*), right aortic arch (*RAA*), left aortic arch (*LAA*), right subclavian artery (*RSA*), left subclavian artery (*LSA*), ductus arteriosus (*DA*), hilus of the right lung (*RL*) and descending aorta (*A*).

B, anterior view, showing the ascending aorta (*AA*), pulmonary artery (*PA*), ductus arteriosus (*DA*), right aortic arch (*RAA*), left aortic arch (*LAA*), right common carotid artery (*RCC*), left common carotid artery (*LCC*), right subclavian artery (*RSA*), left subclavian artery (*LSA*) and trachea (*T*).

the laryngoscope, respiration ceased entirely. This indicated increased tracheal obstruction. However, the larynx was inspected and appeared normal. Tracheoscopic examination could not be carried out because of the complete obstruction of the airway. After the laryngoscopic procedure, respirations began only when the infant was held in the peculiar position previously noted—with the neck extended and with flexion of the head on the neck.

In the hope of improving the airway, a low tracheotomy was performed. Several cubic centimeters of thick pus was aspirated, and the patient experienced some relief. When a small rubber aspirating catheter was passed through the tracheotomic cannula, an obstruction was noted below the end of the cannula at a level about 1 cm. below the suprasternal notch. The catheter would pass this narrowing only with difficulty.

As this location seemed inaccessible to treatment, no further surgical procedures were contemplated. On the second day following tracheotomy, the fifth day of hospitalization, the infant died.

Necropsy.—The pertinent observations were confined to the heart, the aortic arch and its branches, the esophagus, the trachea and the lungs.

The heart was not enlarged. The only abnormality was an anatomically patent foramen ovale which measured 6 mm. in diameter.

The origins of the pulmonary artery and aorta were normal in shape, size and position (fig. *B*). The ascending aorta was anterior to but slightly to the right of the trachea. At its superior portion it bifurcated into a larger right and a smaller left aortic arch, measuring 1.0 cm. and 0.5 cm. in diameter respectively. Each was directed dorsally, lateral to the trachea and esophagus and superior to the hilus of the corresponding lung. Posterior to the esophagus the arches united, forming a complete arterial collar encircling the trachea and esophagus (fig. *A*). The descending aorta was situated slightly to the left of the midline. The great vessels of the neck and upper extremities arose almost symmetrically from each arch. There was no innominate artery. The first branches were the right and the left common carotid artery, arising from the superior portion and the origin of the corresponding arch. The next branches were the right and the left subclavian artery. These originated from the convexity and the most superior portion of each arch at approximately the midpoint between the termination of the ascending aorta and the beginning of the descending aorta. The ductus arteriosus was present. It measured 0.4 cm. in diameter and arose from the distal portion of the main pulmonary artery. It entered the left aortic arch just beyond the origin of the left subclavian artery. All the vessels just mentioned were patent.

The vascular collar definitely constricted the esophagus (fig. *A*) but had produced no ulceration of its mucosa. Constriction of the trachea, however, was less apparent. There was a slight amount of sticky, fibrinopurulent exudate covering the mucosa of the membranous portion of the trachea inferior to the tracheotomy incision.

The lungs grossly did not show any pathologic conditions. Microscopically they showed small patchy areas of partial atelectasis alternating with areas of acute emphysema. There was no pneumonia.

COMMENT

A double aortic arch can be readily explained from a developmental standpoint. Very early in life the human embryo possesses a series of aortic arches which extend from the ventral bulbus arteriosus to the paired dorsal aortas (Jordan and Kindred [4]). This arrangement is temporary. By means of obliteration and absorption, certain portions of these arches disappear, leaving the rather complicated arterial tree which

4. Jordan, H. E., and Kindred, J. E.: A Textbook of Embryology, New York, D. Appleton & Company, 1926, p. 145.

one is accustomed to call normal. Thus, usually, the left portion of the fourth pair of aortic arches persists as the aortic arch, while certain parts of the right portion disappear, leaving a vessel which later becomes the right subclavian artery. In a small number of persons, for some unknown reason, the right fourth aortic arch persists in its entirety, and so when the left arch is also present there is present what is commonly known as a double aortic arch.

That a complete functioning double aortic arch is not incompatible with life is clearly demonstrated by a case recently encountered at autopsy. The patient was a Negro in his late thirties who died of Addison's disease. He had never had any symptoms indicative of either tracheal or esophageal obstruction, and yet he possessed a double aortic arch almost identical with the one in the case just described. In their excellent review of the literature, Blincoe, Lowance and Venable [5] cited 12 additional cases of essentially the same anatomic anomaly in adults. In these cases the lumen formed by the two arches was obviously large enough to permit the passing of the trachea and esophagus without causing constriction.

On the other hand, when the arches form a snug constricting collar about the trachea and esophagus, there are produced a group of rather constant symptoms, as previously outlined. In all the cases of double arch of this type reported, the onset of these symptoms occurred either at birth or very shortly thereafter. Respirations were noted to be of a noisy and wheezy character, and there were paroxysms of coughing with dyspnea and cyanosis. These attacks were usually initiated by feeding or crying. The infant assumed an unusual position, with extension of the neck and pulling in of the chin. In our case, the head was also rotated to the left. Any change from this position apparently embarrassed the airway, as evidenced by increased dyspnea and cyanosis. The progressive malnutrition is apparently due to the continued deficiency in oxygenation plus the difficulty in feeding. Malnutrition and the narrowed airway with its resultant retention of secretions predispose these infants to bronchopneumonic processes. The span of life in the cases observed varied from ten days to six months.

While this group of findings represents only various phases of tracheal and esophageal obstruction, it is suggestive of the presence of a constricting double aortic arch, if this anomaly is kept in mind. The roentgenologist, once his attention is directed to this unusual condition, can offer considerable aid in diagnosis.[6] He not only can rule out most

5. Blincoe, H.; Lowance, M. I., and Venable, J.: A Double Aortic Arch in Man, Anat. Rec. **66**:505, 1936.

6. Sprague, H. B.; Ernlund, C. B., and Albright, F.: Clinical Aspects of Persistent Right Aortic Root, New England J. Med. **209**:682, 1933. Arkin, A.: Double Aortic Arch, Am. Heart J. **11**:444, 1936.

other possible causes but will be able to demonstrate a number of rather conclusive features. The broadening of the superior mediastinal shadows, often very slight, can then be investigated thoroughly. However, the characteristic esophageal constriction at the level of the aortic arch [7] is the most constant and the most informative manifestation. This is best demonstrated by fluoroscopic studies of the swallowing function followed by roentgenograms of the outlined esophagus.

Although Schall and Johnson [2] were able to demonstrate the constriction of the trachea by means of bronchoscopic examination, this procedure was not feasible in the case reported, because of the marked obstruction of the airway when the infant was held in any position approximating that necessary for this operation. Esophagoscopic examination is contraindicated, since it further embarrasses an already embarrassed airway.

Tracheotomy is helpful only in that it allows removal of accumulated secretion below the constricted area.

The recent work of Gross and Hubbard [8] gives impetus to the hope that a successful surgical procedure may be developed which will sever the constricting vascular ring. This, however, is entirely dependent on the establishment of a relatively early diagnosis.

SUMMARY

A case of a constricting double aortic arch incompatible with prolonged life is reported. A constant symptom complex does exist, and recognition of this, supplemented by suitable roentgenographic studies, offers definite diagnostic possibilities. The possibility of a successful surgical treatment is suggested.

Jefferson Hospital.

7. Garland, F. L.: Persistent Right Sided Aortic Arch, Am. J. Roentgenol. **39**:713, 1938.

8. Gross, R. E., and Hubbard, J. P.: Surgical Ligation of Patent Ductus Arteriosus: Report of First Successful Case, J. A. M. A. **112**:729 (Feb. 25) 1939. Gross, R. E.: Surgical Management of Patent Ductus Arteriosus with Summary of Four Surgically Treated Cases, Ann. Surg. **110**:321, 1939; Experiences with Surgical Treatment in Ten Cases of Patent Ductus Arteriosus, J. A. M. A. **115**:1257 (Oct. 12) 1940.

Case Reports

BILATERAL POLYP OF THE FAUCIAL TONSILS

Report of a Case, with Review of the Literature

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True polyp of the tonsil being rather a rare lesion, this report of a case may prove of interest. A review of the recent literature on the subject reveals that New and Childrey [1] reported 357 cases of tumors of the tonsil and pharynx seen at the Mayo Clinic from 1917 through 1930. Of these tumors, 63 were benign and in the latter group only 2 polyps were observed. Of these 2 polyps, 1 proved to be a malignant dermoid and the other a fibromyxomatous polyp springing from the posterior wall of the pharynx just above the glottis. No polyps springing from the tonsil itself were observed in this series.

Smith [2] reported a study of the microscopic pathology of the palatine tonsil in a series of cases seen at the Massachusetts Eye and Ear Infirmary from Sept. 1, 1933 to Sept. 1, 1934. During the year tonsillectomy was done in 2,200 cases. In 30 of this number a pathologic process other than the usual chronic infection appeared to be present, and the tonsils accordingly were sent to the laboratory for pathologic study. In none of these tonsils was there evidence of a polyp.

Evans and Odom [3] reported a case of a true benign polyp which was attached to the superior pole of the right tonsil of a girl 13 years of age.

REPORT OF CASE

A. P. R., a white man aged 38, was transferred from the clinic to the medical service of Roper Hospital on April 22, 1942 with the history of a cough of four years' duration which was productive of mucoid material. He denied having hemoptysis, night sweats, dyspnea or any other symptoms referable to a pathologic condition of the lung. He stated that he had never been free of an uncomfortable feeling in the throat during the four years. There had been no loss of weight up to the past six weeks, but since that time he had lost about 20 pounds (9.1 Kg.).

Physical examination revealed that the patient was well developed and well nourished. Examination of the throat showed an ovoid tumor, approximately 2 cm. long by 1 cm. wide, attached by a broad base to the superior pole of the left

1. New, G. B., and Childrey, J. H.: Tumors of the Tonsil and Pharynx (Three Hundred and Fifty-Seven Cases): I. Benign Tumors (Sixty-Three Cases), Arch. Otolaryng. **14**:596-609 (Nov.) 1931.

2. Smith, H. D.: Microscopic Pathology of the Palatine Tonsil, Arch. Otolaryng. **21**:426-436 (April) 1935.

3. Evans, W. H., and Odom, R. E.: Polyp of the Tonsil: Report of a Case, Ann. Otol., Rhin. & Laryng. **48**:495-498 (June) 1939.

tonsil and extending medially to touch the uvula. It was firm and presented a smooth, glistening surface. The cervical nodes were not enlarged.

The remainder of the examination revealed essentially normal structures.

Consultation with the otolaryngologic service was requested, and I saw the patient on April 24. The previous observations were confirmed, and a tonsillectomy with local anesthesia was advised. This was performed on May 4 by sharp and blunt dissection and snare. No ties were required.

The patient made a prompt and uneventful recovery, and on discharge to the clinic on May 9 he was practically free of cough. Subsequent examination in the clinic on May 15 revealed a normal post-tonsillectomy condition, and the cough had entirely disappeared.

Microscopic examination of a section of the tumor revealed a vascular, fibrous polyp. The other tonsil also contained a smaller similar mass in its substance. A slide of the mounted specimen was forwarded to the Army Medical Museum in Washington, D. C., for diagnosis, and the aforementioned observations were confirmed.

SUMMARY

A brief review of the recent literature on polyps of the tonsil indicates the rarity of this lesion. A case presenting this pathologic condition in both tonsils is reported. Tonsillectomy was performed, with the result that the patient was relieved of his symptoms.

96A Bull Street.

CHOLESTEATOMATOUS EXPOSURE OF THE SIGMOID SINUS THROUGH THE POSTERIOR OSSEOUS CANAL WALL

ISIDORE BERGER, M.D., NEW YORK

This case report is interesting since a survey of the literature did not reveal any record of a similar pathologic finding.

E. H., a white woman aged 26, sought examination July 26, 1941, because of a purulent odorous discharge from the right ear, as well as poor hearing and occasional bleeding since early childhood. Alternating periods of exacerbation and improvement followed rhinopharyngeal and sinal infections. Examination of the right ear revealed the following: The auricle and cartilaginous canal were normal. Some tenderness was present over the mastoid process. The posterior osseous canal wall showed a large defect through which a large vascular grayish blue bulge (anterior vertical part of the sigmoid sinus) projected into the lumen of the canal. Brownish red pigmentation with slight superficial ulceration, from which some bleeding occurred on mild manipulation, was also noted over this vascularity.

The cholesteatomatous process had destroyed part of the posterior canal wall, the sinus plate, the ossicles and the drum membrane, fusing the mastoid antrum, the middle ear and the external auditory canal into one cavity. Fibrosis had taken place over part of the drum membrane. More deeply toward the labyrinthine wall of the middle ear, a glistening small mass, possibly part of the cholesteatoma, appeared.

Drs. Wells P. Eagleton and Lester M. Hubby communicated their findings as follows:

Dr. Eagleton's comment: "Coming from the posterior wall forward, just this side of the middle, there is a mass which appears to be a blood vessel because when I touch it there is a hemorrhage into the wall. It is, however, too firm to be simply a blood vessel coming from the floor. Beyond this I can see the remains of the middle ear; it is a glistening mass, like a cholesteatoma, and yet I do not think it is."

Dr. Hubby's comment: "There appears to be a cholesteatomatous cavity in the right temporal bone, in which the bone over the anterior half of the vertical portion of the sigmoid sinus, the annulus and the ossicles have disappeared.

"The exposed portion of the sigmoid sinus is blue and thin. There is a thin scar-tissue-like membrane over the anterior half of the tympanum. The rest of the tympanum and attic appear to be bony and covered with a thin layer of epithelium."

Roentgenograms revealed sclerosis with obliteration of the right mastoid cells. Dr. Eagleton also found an area of increased radiability in the upper portion of the right mastoid process, possibly due to a cholesteatoma.

Treatment consisted of gentle cleansing and insufflation of sulfanilamide powder during the period of discharge. Extreme caution against trauma and manipulation was advised.

888 Grand Concourse.

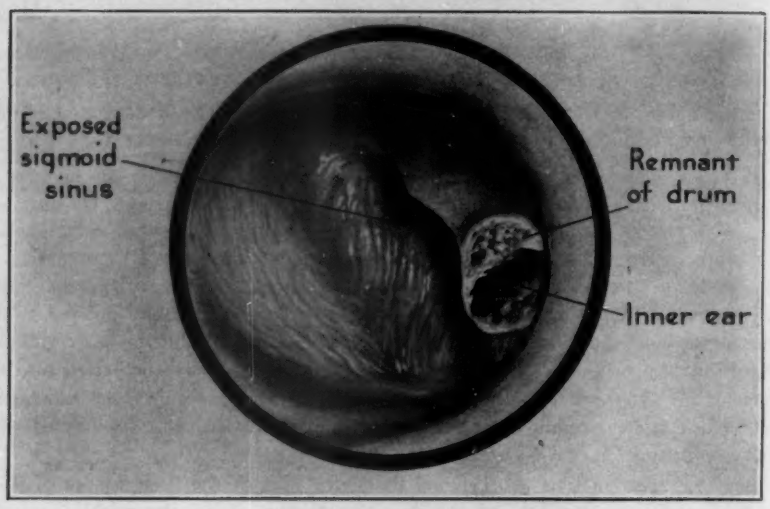

Fig. 1.—Otoscopic view (magnified).

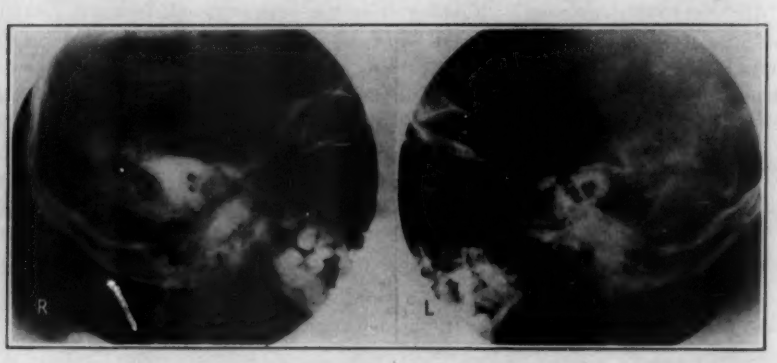

Fig. 2.—Roentgenograms of the right and left mastoid regions.

Progress in Otolaryngology

Summaries of the Bibliographic Material Available in the Field of Otolaryngology

ANATOMY AND PHYSIOLOGY OF THE EAR

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In reviewing the American and British literature available from November 1941 to December 1942 pertaining to the anatomy and physiology of the ear, summaries and abstracts of articles are presented which permit the reader in a brief time to obtain a panorama of the field concerned. This review is not intended to be self sufficient, as are the original papers. Only articles that seem of special value are included.

AVIATION PHYSIOLOGY

Many new physiologic problems have arisen in the present world war. Aircraft motor power has been greatly multiplied, speed sharply increased and ceilings tremendously elevated. Papers, such as those of Kos,[1] Carson[2] and Campbell,[3] discuss the otolaryngologic problems involved.

In his discussion of the otologic problems in the order of their importance, Campbell[3] says the first is the selection of candidates.

> A candidate can become a good airman if he simply possesses a nose of average normal function, average ears and hearing, and eustachian tubes and sinuses without obstruction. His balance mechanism must be within the normal range and he must be without danger of vertiginous episodes. Experience has proven these requirements to be adequate. Through training he can be taught to ventilate his middle ears in rapid descent. He can learn what illusions to expect from his balance mechanism and to rely upon instruments for special orientation. He can be admonished not to fly with nasopharyngitis or sinusitis. Although often a skeptic he will become a firm believer after his first violation of that axiom.

For a more detailed description of the present otolaryngologic standards for Army and Navy pilots Fenton's[4] article is illuminating.

1. Kos, C. M.: Otolaryngological Problems in Aviation Medicine, Texas State J. Med. **38**:281-284 (Aug.) 1942.
2. Carson, L. D.: Otolaryngological Aspects of Aviation, Laryngoscope **52**: 704-717 (Sept.) 1942.
3. Campbell, P. A.: Otolaryngological Problems of Aviation in World War Two, Ann. Otol., Rhin. & Laryng. **51**:293-300 (June) 1942.
4. Fenton, R. A.: Otology and Aviation, Ann. Otol., Rhin. & Laryng. **51**:333-342 (June) 1942.

The second problem, according to Campbell,[3] is to "keep the hearing of air crews at a high degree of efficiency at all times. The information gained through their ears is absolutely essential for flying." The radio beam, weather reports, intercrew communications and motor rhythm must be heard easily. Changes in altitude and fatigue in the organ of Corti due to noise result in continued alterations in the curve of hearing. Aircraft noise can produce a 15 decibel loss in the 3000 to 5000 frequency area in one hour and a 25 decibel loss after four hours of flight. Fortunately, most hearing losses are transitory and after a few hours of quiet usually return to normal. There are great individual variations. Audiograms of aviators are influenced by several factors. First, the higher frequencies show a progressive drop with increased age. Second, continued auditory trauma may cause a loss for the high tones, with its greater influence in the frequencies between 3000 and 5000. Third, changes in barometric pressure influence hearing for the entire range of frequencies; increased pressure causes a general lowering of the curve.

Dickson[5] briefly discusses this second problem and expresses the belief that the flying helmet with telephones attached is the best solution and affords fullest protection against the development of deafness. Kos[1] and others agree.

Fry[6] feels that the hearing tests used for aviation candidates, threshold testing with pure tones, are not adequate. The noise background present in flying is omitted. Thus Fry advocates gramophone records in which test words or sentences are spoken against a noise background. These are delivered to the candidate's ear phones. The noise level can be varied and acoustic conditions for testing standardized. An obvious advantage is that a number of candidates can be examined at the same time.

The third problem stressed by Campbell is aero-otitis-media. While little difficulty is experienced in ascent, sudden descent may result in forcing together tightly the epithelium of the eustachian tube. If yawning, swallowing, etc., fail to open the tube before the negative pressure of 100 to 200 mm. is reached, the epithelium becomes locked tightly.

A cycle of events is then initiated resulting in aero-otitis. When the negative pressure inside the middle ear reaches 100 to 200 mm. of mercury the pain rather suddenly becomes quite severe, 10 or more decibels of hearing is lost usually in some portion of the low tone range (128 dvb. to 2048 dvb.) varying among individuals. On examination the drum is seen to be sharply retracted and there is engorgement of the vessels along the handle of the malleus. A few minutes later

5. Dickson, A. D. D.: Aviation Noise Deafness and Its Prevention, J. Laryng. & Otol. **57**:8-10 (Jan.) 1942.

6. Fry, D. B.: A Suggestion for a New Method of Testing Hearing in Aviation Candidates, J. Laryng. & Otol. **57**:11-13 (Jan.) 1942.

ecchymosis may appear in Schrapnell's membrane and along the lower aspect of the handle of the malleus. After a period of from one-half hour to eight or ten hours depending upon the degree of differential pressure, serosanguineous fluid and bubbles form in the middle ear.

The formation of space-filling fluid from the mucosal lining initiates the beginning of the recovery cycle as the relative negative pressure or vacuum is reduced in proportion to the fluid which forms. After a period pressure is equalized and the flutter valve is released. The structures of the ear which may have been altered to some extent by this barotrauma may take from three to twenty-one days for complete recovery. Fortunately only a very few become infected. Unfortunately, in my experience at least, Politzeriation and catheterization are of little value unless performed immediately and then are not always efficient. The most effective treatment is for the individual to return to the level at which the block occurred either in actual flight or in a pressure chamber, and then to return to ground level very slowly swallowing frequently on the descent. In this manner both the pressure outside of the drum and the pressure of the air passing through the eustachian tubes are altered simultaneously. . . . If aero-otitis has existed over a period of a few hours the only other alternative is to use heat to increase fluid production in the middle ear, analgesics for the relief of pain, and shrinking medication to the orifice of the eustachian tube. Paracentesis, I believe, is absolutely contraindicated.

McGibbon,[7] writing about this syndrome, aero-otitis-media, states that 26 per cent of the total number of air crew personnel referred to the department of otorhinolaryngology of a Royal Air Force general hospital have complained of aural symptoms which arose during loss of height while flying. The author reviews 100 cases.

Proof of blockage of the eustachian tubes is based on presumptive and on positive evidence. As presumptive evidence, 94 aviators complained of deafness, and probably had the other 6 men been examined sooner after landing, a deficiency in hearing would have been found. Normal drum heads were seen in 26 patients, while invagination of the tympanic membrane to a varying degree was the most common finding, this being noted in 47 patients. Congestion of the attic was present in 6 patients, and congestion of the entire drum head was noted in 8 patients. These two conditions simulate and are often mistaken for acute bilateral otitis media. Effusion into the tympanum was seen in 6 patients. Rupture of the drum head was present in 7 patients.

As positive evidence, there is the fact that Valsalva's method alone or combined with swallowing movements will not open the tube. With the eustachian catheter in the tubal orifice, the maximum pressure at its tip has been estimated to be 320 mm. of mercury. In only 1 patient was inflation by eustachian catheter successful at the first visit. An attempt to pass a tympanic sound or catheter was made with 57 patients, and in all the passage of the instrument was arrested by a firm

7. McGibbon, J. E. G.: Aviation Pressure Deafness, J. Laryng. & Otol. **57**: 14-22 (Jan.) 1942.

obstruction at a distance varying from 0.5 to 2 cm. from the tip of the catheter. Roentgenologic evidence of obstruction after the injection of a radiopaque fluid into the eustachian tube was demonstrated in 36 patients of this series. In 2 patients the obstruction was at the isthmus; in 1, 0.5 cm. from its pharyngeal orifice, and in the remaining 33 patients, at intermediate situations.

The author describes the normal anatomy and physiology of the eustachian tube. His conception is that the tube is opened in a sinuous manner by the combined action of the sphincter of the pharyngonasal isthmus and of the upper part of the superior constrictor muscle, which drag the posteromedial cartilaginous wall inward, while simultaneously the tensor palati muscle braces the anterolateral wall against the medial pterygoid lamina and draws down the hamular process of the cartilage to relax the membranous wall. Three excellent diagrams clarify the author's words.

Ventilation of the middle ear during flight occurs during ascent as a "click," and air escapes from the eustachian tube easily and automatically each 425 feet (130 meters). During loss of height in flying or increase of pressure when the subject is in a chamber, the eustachian tube behaves in an entirely different manner, for even with a normal tube air does not enter the middle ear automatically. In the majority of aviators, however, the tube is opened, and ventilation of the middle ear is brought about by involuntary swallowing movements, which occur at the rate of once every sixty to seventy-five seconds in normal persons.

Nonventilation of the middle ear during descent results either from failure or inability to open the tube. If from any cause ventilation of the middle ear does not take place during loss of height, a positive pressure, depending on the amount of loss and the altitude at which it occurs, develops outside the middle ear cleft. Armstrong and Heim [8] (1937) have shown that a extratympanic positive pressure of 90 mm. of mercury or more will cause the tube to "lock," as the muscles concerned are unable to overcome this force. This occlusion due to pressure McGibbon calls primary (pressure) occlusion. If "forced ventilation" of the middle ear is not available or is neglected for more than one or two hours, the tube becomes impermeable to air even at high pressures and to fluids and sounds.

It is reasonable to assume, therefore, that some biologic change has taken place as a result of the primary (pressure) occlusion, and this McGibbon calls secondary (vital) occlusion. The nature of these secondary changes is not known, but it can be surmised when one views the thickness of the submucosa and the large number of mucous glands

8. Armstrong, H. G., and Heim, J. W.: Effect of Flight on Middle Ear, J. A. M. A. **109**:417-421 (Aug. 7) 1937.

and goblet cells which are present in the epithelial lining of the cartilaginous tube. Secondary occlusion is a real entity, and it may take as long as fourteen weeks to resolve, as happened in 1 patient of this series.

The effect of simple occlusion of the eustachian tubes on hearing was investigated by Loch.[9] Inflation of a soft rubber balloon in the nasopharynx was used to obstruct the eustachian tubes. The hearing was repeatedly tested during the next one and one-half hours, a Western Electric 1-A audiometer, which produces frequencies from 32 to 16384 cycles per second, being used.

This purely mechanical occlusion of the eustachian tubes caused first and chiefly hearing impairment in the high tone region. Later the hearing for low and middle tones became slightly impaired. Immediately after restoration of adequate ventilation of the middle ear (removal of the balloon, a positive response to the Valsalva procedure and swallowing) the hearing threshold for all frequencies returned to the values obtained before placement of the balloon.

The prompt recovery of hearing acuity proved that secondary changes, such as edema of the organ of Corti or of the round window membrane, could not have been responsible for the impairment, which can only be explained as a result of pressure changes in the middle ear following the experimental occlusion.

These experiments confirm the clinical impression of Crowe and Guild that an uncomplicateld tubal occlusion causes a hearing loss for high tones, sometimes followed by impairment for other tones also.

Tubal occlusion must be considered as one of the causes of impaired hearing for high tones. The fact that the original hearing can be restored emphasizes the importance of early recognition and treatment of patients with impaired hearing of this type.

The fourth problem presented by Campbell [3] is air sickness. He claims that there is no simple remedy and asserts that the best protection remains in the selection of candidates.

Kos [1] agrees that vestibular tests, although not entirely reliable, aid materially in the selection of applicants. Simpson,[10] on the other hand, finds vestibular tests of little value. Blind flying by instruments has done away with the false impressions received from the labyrinth in flight, and rotation tests fail to detect persons susceptible to intractable air sickness.

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9. Loch, W. E.: The Effect on Hearing of Experimental Occlusion on the Eustachian Tube in Man, Ann. Otol., Rhin. & Laryng. **51**:396-404 (June) 1942.

10. Simpson, J. F.: A General Survey of Otorhinological Considerations in Service Aviation, J. Laryng. & Otol. **57**:1-7 (Jan.) 1942.

Winfield [11] records certain observations on air sickness. When one flies for the first time, the labyrinth is subjected to a series of new stimuli caused by unaccustomed motion of the aircraft. The effect of these stimuli is to cause sweating, pallor, nausea and malaise, which may be followed by vomiting. Five to 10 per cent of men who fly for the first time vomit more than once during their first twelve hours in the air. In the vast majority, however, physiologic adaptation occurs, and air sickness will then recur only if this adaptation is broken. This may be caused by prolonged severe aerobatics, by a change in the type of aircraft flown, by absence from flying for about six months or, again, by flying in very rough weather. The incidence of air sickness is influenced by the accessory factors—weather, type of aircraft, noise and vibration, ventilation, comfort, diet, ocular stimuli, cold, anoxia and boredom. The presence of any form of organic disease will increase liability to air sickness. The more common conditions associated with it are sinusitis and otitis, and when these have been cured air sickness ceases. It is interesting to note that when a pilot is flying the aircraft himself he is rarely sick. But some pilots become sick when flying with the automatic pilot, which anticipates the aircraft movement for them.

Drug therapy is limited by the fact that, whatever drugs are used, cortical function must not be depressed. Treatment, therefore, is directed mainly toward taking care of the accessory factors.

The last problem mentioned by Campbell [3] is the effect of anoxia on hearing. This is important at the higher altitudes. The anoxia affects the higher centers and in some respects is similar to acute alcoholism.

The aforelisted problems affect especially those who fly; it must be remembered that aero-otitis-media occurs in caisson workers, as described by Almour.[12] Likewise, Shilling and Everley [13] describe the occurrence of aero-otitis-media in submarine personnel. They also emphasize hearing losses due to exposure to the noise of Diesel engines operating in a confined space. Hearing for the higher frequencies showed the greatest loss. The longer the auditory trauma the greater the loss demonstrated. This held true in the case of radio men using ear phones under severe conditions.

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11. Winfield, R. H.: Observations on Air-Sickness, J. Laryng. & Otol. **57**: 23-25 (Jan.) 1942.

12. Almour, R.: "Blocked Ear" of the Caisson Worker, Laryngoscope **52**: 75-81 (Jan.) 1942.

13. Shilling, C. W., and Everley, I. A.: Auditory Acuity Among Submarine Personnel, U. S. Nav. M. Bull. **40**:27-42 (Jan.); 396-403 (April); 664-685 (July) 1942.

DEVELOPMENTAL ANATOMY

In another contribution from his studies on the development of the otic capsule, Bast [14] describes the histologic changes and variations in the growing bony capsule of the vestibule and cochlea. The otic capsule consists of three layers of bone, the periosteal, the endosteal and the middle, or so-called endochondral, layer. The histogenesis of each layer is described. The periosteal and endosteal layers develop much the same as in other bones. The basic, or fundamental, layer, the middle layer, develops and possesses structural factors different from those of other bones of the body. The essential steps in the osteogenesis of this middle layer in the cochlear portion of the capsule are described as follows:

> The earliest ossification center appears at about 16 weeks [of fetal life] in the capsule over the base of the cochlea near the round window. During the next week or two, five ossification centers appear around the internal auditory meatus and one in the roof of the cochlea. From these centers ossification progresses very rapidly so that by the twenty-first week the capsule around the cochlea is well ossified except for a small area (the fissular area) between the vestibule and the cochlea and an area medial to the cochlea where the cartilage continues to grow to form the petrous apex. . . . In the process of ossification the following changes occur:
>
> The cartilage cells enlarge, [then shrink and disintegrate] and the matrix between the cells becomes calcified. . . .
>
> With the calcification of the matrix, the perichondrium becomes the periosteum. The cells of this periosteum which lie next to the calcified cartilage matrix change into osteoblasts. Some of these osteoblasts begin to form periosteal bone and others wander into the opened and enlarged cartilage lacunae. . . . While this goes on osteogenic buds invade the changed cartilage, opening large spaces but leaving considerable masses and strands of the calcified cartilage and the enclosed lacuna containing the newly acquired bone. . . . This intrachondrial bone formed in the first week of the ossifying process is a permanent tissue and remains throughout life as a part of the middle layer of the otic capsule.
>
> Little change occurs in the middle layer from the twenty-first to about the twenty-sixth week. Osteoblasts line up at the margin of the evacuated spaces on the surface of the intrachondrial bone. These osteoblasts then deposit endochondral or replacement bone on the surface of the intrachondrial bone. Endochondral ossification is slow during the rest of fetal life and at birth the middle layer may still have large marrow spaces. At about birth the process speeds up and within a few months the ossification of the middle layer is pretty well completed. The composition of the middle layer obtained at this stage is retained throughout life. Up to about the seventh month of postnatal life, the boundary of the middle layer is quite distinct from the periosteal layer and as a result is not firmly united to the rest of the petrous bone. To accomplish this union resorption of part of the middle and periosteal layers takes place and these evacuated areas are then filled in with new bone, thus knitting the two layers firmly together. . . .

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14. Bast, T. H.: Development of the Otic Capsule: VI. Histological Change and Variations in the Growing Bony Capsule of the Vestibule and Cochlea, Ann. Otol., Rhin. & Laryng. **51**:342-356 (June) 1942.

In the evaluation of the significance of the endosteal, periosteal, and middle layers of the otic capsule, the time and speed of their development and the role they play in the composition of the capsule seem worthy of consideration.

The endosteal and periosteal layers . . . begin to develop early in the ossifying process. The endosteal layer increases in size but very little after it is first laid down. Throughout life it remains as a thin layer which is fairly uniform in thickness in all parts of the capsule.

The periosteal layer begins at the same time but develops very rapidly into a very prominent part of the otic capsule. . . . The periosteal bone reaches its maximum growth at about the time when the endochondral bone of the middle ear begins to be formed. It appears that at about the twenty-seventh week there is a shift of bone deposition from the periosteal layer to the formation of the endochondral or replacement bone around the intrachondrial of the middle layer. Even this endochondral bone formation is slow so that by the thirty-ninth week the middle layer still has much bone marrow and bone spicules are only slightly larger than at 27 weeks. . . . Immediately after birth the bone marrow of both the middle layer and periosteal layer is rapidly replaced by bone. Thus, in a 7-month-old child both layers are made up of compact bone except for re-excavated areas between the two layers. By the third year all the layers consist of compact bone and the lines marking the three layers are obliterated.

Special attention is called to the area anterior and medial to the oval window and between the vestibule and the cochlea. This area is often referred to as the fissular area, for it is here that the fissula ante fenestram occurs. Here the capsule is made up almost entirely of the middle layer, and only a very thin periosteal layer separates the middle layer from the tympanic cavity. It is further of interest that it is in this region that otosclerotic foci are usually encountered and that ankylosis of the stapes begins. In 1940 Bast [15] showed that residual cartilage, neoplastic cartilages or defective ossifications occur at various specific spots in the otic capsule. The unstable spots always occur in the middle layer and where it is prominent. The indication, therefore, is that this middle layer is the more unstable type of bone and it may be subject to subsequent changes. Otosclerotic foci have been associated with such areas, and it would be of interest to know whether any of the other pathologic processes may have their starting points in these areas.

Pneumatization of the petrous pyramid is clarified and simplified by Lindsay.[16] In a brief paper he presents an excellent series of semidiagrammatic illustrations. The simplest clinical classification of suppuration of the petrous pyramid is the division into posterior and anterior petrositis, the former occurring with pneumatization by the posterior route, the latter with pneumatization by the anterior route.

15. Bast, T. H.: Development of the Otic Capsule: V. Residual Cartilages and Defective Ossification and Their Relation to Otosclerotic Foci, Arch. Otolaryng. **32**:771-782 (Oct.) 1940.

16. Lindsay, J. R.: Pneumatization of the Petrous Pyramid, Ann. Otol., Rhin. & Laryng. **50**:1109-1113 (Dec.) 1941.

In the author's experience the relative frequency has been: posterior petrositis, 70 per cent, and anterior petrositis, 30 per cent. The possible surgical approaches in cases of each type have been indicated in the legend beneath each illustration, as well as by the roentgenographic projection which is most suitable to demonstrate the area. The illustrations are based on and correlated with previous reports on the anatomy and pathology of the petrous pyramid.

Garlichs and Griffith [17] continue their studies in a paper on lymphatic absorption from the auditory bulla of the rat with special reference to the lateral sinus. They injected thorium dioxide into the auditory bulla of the rat, and subsequently histologic sections showed the substance in the perisinal space of the lateral sinus. This space, as well as other perisinal spaces in the skull, may function as a lymphatic channel. The importance of these spaces in the spread of infection is evident—for example, in mastoiditis. Otologists are familiar with the development of mural thrombi and with complete thrombosis of the lateral sinus subsequent to mastoiditis. Perhaps more often than is realized infection may block the normal route of perisinal absorption from the cerebrospinal space. Thus simple surgical exposure of a lateral sinus drains this perisinal space and prevents spread of infection. This would explain the rapid recovery after exposure of a normal lateral sinus of patients with mastoiditis who present clinical signs of intracranial extension.

The authors' concept of the absorption of cerebrospinal fluid, which differs from the conventional theories, is as follows:

1. The pacchionian bodies and special sinal structures have no function in effecting absorption of cerebrospinal fluid. Insofar as such fluid is absorbed into the blood stream, it enters vessels of capillary size, as it does everywhere else in the body. 2. An important and necessary part of the cerebrospinal fluid is absorbed through channels, either perineural or perivascular, which lead to systemic lymphatics. This mechanism may be described as lymphatic absorption and effects the disposal of all particulate matter, as does the lymphatic system generally. The route for particulate matter released over the hemispheres of the brain would be, for example, along perivascular spaces to the perisinal space of the superior longitudinal sinus and thence along corresponding spaces to the perisinal space of the torcular Herophili, the lateral sinus and the jugular vein, to reach finally the cervical lymph nodes. If this view is correct, the perisinal space must be considered in problems of infection of the cerebrospinal space and its coverings.

17. Garlichs, R. W., and Griffith, J. Q.: Lymphatic Absorption from the Bulla of the Rat, with Special Reference to the Lateral Sinus, Arch. Otolaryng. **36**:226-231 (Aug.) 1942.

COCHLEAR PHYSIOLOGY

Walzl and Bordley [18] have developed a technic which has repeatedly enabled them to destroy selected regions of the organ of Corti without traumatizing other areas or causing escape of endolymph. The latter point is extremely important in obtaining consistent results, because simple puncture of the cochlear duct in the basal turn causes marked impairment of cochlear potentials for all frequencies. In cats the bone is removed over the selected part of the spiral ligament, which is then further loosened by gentle pressure with a blunt needle. This causes the basilar membrane in this restricted area to bend and the organ of Corti resting on it to be crushed or dislodged. Histologic examination confirmed that the lesions were restricted to the organ of Corti and that both Reissner's and the basilar membrane had remained intact. Graphic reconstructions were made from serial sections to determine the exact location of each lesion.

Single small lesions resulted in moderate impairment of response limited to a small part of the frequency range. Larger lesions caused a greater degree of impairment and involved a wider part of the tonal range. In none of the experiments was there complete loss for any tone, even though histologic examination showed that the organ of Corti was completely destroyed in the region of the detachment. This indicates that the cochlea does not behave as a series of sharply tuned resonators but rather that, as the intensity of a sound is increased, regions of the organ of Corti other than the ones of optimal response are stimulated.

These experiments show that (1) with intensities near threshold the response to any frequency is localized to a small part of the organ of Corti, but with increase in intensity there is spread of the response to the adjacent areas, the spread being greater for low than for high tones; (2) the regions of optimal response for successive octaves are spaced at equal distances along the organ of Corti, and (3) the close correspondence between localization for cochlear potentials in the cat and for hearing in man indicates that cochlear potentials originate in the hair cells of the organ of Corti.

As a result of traumatic damage the organ of Corti degenerates and is absorbed. The mechanism of this process was investigated by Lurie.[19] A large number of guinea pigs and mice were studied. In animals that have had surgical operations on the cochlea, the degenera-

18. Walzl, E. M., and Bordley, J. E.: Effect of Small Lesions of the Organ of Corti on Cochlear Potentials, Am. J. Physiol. **135**:351-360 (Jan.) 1942.

19. Lurie, H. M.: The Degeneration and Absorption of the Organ of Corti in Animals, Ann. Otol., Rhin. & Laryng. **51**:712-717 (Sept.) 1942.

tion of the organ of Corti at the region of the lesion is coincident with an ingrowth of fibrous tissue into the scala media, the scala tympani and the scala vestibuli. With the ingrowth of fibrous tissue new vessels grow in and new formations of tissue take place. In other parts of the cochlea the organ of Corti degenerates and may be absorbed completely without the presence of any fibrosis or any infiltration of endothelial or phagocytic cells. In fact, the cells of the organ of Corti seem to melt away. Animals exposed to the traumatic effects of an intense tone also showed degeneration and absorption of the organ of Corti. There was no evidence of any invasion by fibrous tissue or endothelial cells of any of the scalae of the cochlea. There were no phagocytic cells in the scala media in the region where the lesion was produced. The organ of Corti, which had been thrown off from the basilar membrane, had disappeared, and no evidence or trace of it could be found in the scala media. In either direction from the lesion produced the organ of Corti was degenerating and in various stages of absorption.

The tectorial membrane in all the animals studied was not involved in this process and appeared to be unaffected by the changes occurring in the scala media. The stria vascularis is usually normal, or if there are changes, they do not give any clue as to what occurs in the organ of Corti. The cochlear nerve from the organ of Corti to the spiral ganglion does not begin to degenerate until two or three weeks after the degeneration of the sensory hair cells. At present the only conclusion that can be drawn from these studies is that molecular disintergration of the cells of the organ of Corti takes place. The chemical constituents of the cells dissolve into the fluid of the scala media.

Pohlman [20] presents further objections to the accepted interpretations of cochlear mechanics. He points out why it is wrong to assume that transverse vibrations of the basilar membrane occur and insists that the present generally accepted theories of audition do not fit established facts. The author believes that the auditory cells react directly to vibrations applied directly through the labyrinth fluid.

MacNaughton-Jones,[21] in an elaborate discussion of cochlear resonance, starts with transverse vibrations of the basilar membrane as an established fact. He theorizes on the various steps involved in the physiology of hearing, beginning with the invagination of the round window and continuing all the way through to the generation of the nerve impulses by the hair cells.

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20. Pohlman, A. G.: Further Objections to the Accepted Interpretations of Cochlear Mechanics, Arch. Otolaryng. **35**:613-622 (April) 1942.

21. MacNaughton-Jones, H.: Cochlear Resonance, J. Laryng. & Otol. **57**:193-217 (April) 1942.

Kobrak and associates [22] attempt to analyze the complex phenomenon of auditory masking by comparison of hearing sensations and reflex responses. While the hearing sensation involves the peripheral sense organ as well as higher centers, the acoustic reflex of the muscles of the middle ear is independent of the cortex. Masking can be defined as the raising of the threshold of hearing due to the presence of a second tone. The measure of masking is the number of decibels that the threshold of the masked sound is elevated in consequence of the effect of the masking tone. Similarly, any interference with the threshold of the tensor tympani reflex by a second sound can be determined experimentally.

The authors found that in the rabbit the acoustic reflex of the tensor tympani muscle is unchanged in the presence of the typical room noise background or when a masking tone is sounded which is below the threshold of the reflex. If the masking tone is above this threshold, the acoustic contractions of the tensor tympani muscle are superimposed. The threshold is raised.

In human subjects the acoustic reflex of the stapedius muscle has been observed under the influence of masking. Audiometric curves are presented which show the dip in hearing sensation due to masking, without a change in the threshold of the stapedius reflex. The absence of the masking effect on the acoustic reflex of the middle ear indicates that masking originates outside the part of the acoustic system in which hearing sensation and reflex responses are located. From these experiments on the reflex contractions, the conclusion is drawn that the mechanical stimulation of the cochlea is undiminished in the presence of the masking tone. Since both reflex contractions and cochlear potentials are unchanged, the origin of masking is most likely not in the peripheral sense organ.

Senturia and Thea [23] describe the technic of bone conduction in audiometry. They find that bone conduction curves give a more direct picture of cochlear function than air conduction curves. The most vulnerable portion of the bone conduction curve appears to be located at 4096 double vibrations and the most resistant below 1024 double vibrations. Evidence is presented which favors the theory of direct osseous transmission of bone-conducted sound.

The discrete frequency audiogram is now generally accepted as the measure of hearing acuity. It measures the improvement resulting from any type of therapy. It is the basis for the much discussed per-

22. Kobrak, H. G.; Lindsay, J. R., and Perlman, H. B.: Experimental Observations on Auditory Masking, Laryngoscope **52**:870-878 (Nov.) 1942.

23. Senturia, B. H., and Thea, A. R.: Bone Conduction in Audiometry: I. Literature Review and Report of Preliminary Observations, Laryngoscope **52**:675-686 (Sept.) 1942.

centage loss of hearing. Essentially the audiogram represents the threshold of hearing for a series of frequencies arranged in octave steps from 128 to 8192 cycles. However standard the use of the discrete frequency audiometer has become as a method of measuring hearing loss, it still leaves many questions unsettled. Chief of these is the relation of this threshold audiogram to a practical disability imposed by a given hearing loss. "We do not live in a world of threshold sound" is the commonest criticism advanced. "The relationship between the audiogram and the ability to understand speech is obscure" is another.

During the past three years Hughson and Thompson [24] have conducted an important study designed, first, to establish a normal threshold for hearing of speech as related to normal audiograms and, second, to establish a simple and straightforward method of correlating audiograms for impaired hearing with actual hearing disability for speech. The method by which this work was done involves the use of a reader, a microphone and an amplifier in a soundproof booth, with the operator and the subject in a soundproof room containing a loud speaker, ear phones and an attenuator. The procedure is simply and clearly reported and is supplemented by charts and composite audiograms based on 104 normal ears and 87 ears with impaired hearing.

As a result of this study a normal level for the threshold of audibility for speech reception (or the ability to understand speech) is established, and contrasted with it are the values for a series of groups of persons presenting varying degrees of impairment. A definite correlation between the audiometric percentage loss and the percentage loss for speech has been determined. Though unequal in actual degree, the relationship remains constant throughout the entire audiometric range of intensities, the former representing percentage loss of total hearing and the latter percentage loss for speech. For example, a 20 per cent audiometric loss means a 40 per cent loss for speech reception. Bone conduction and nerve deafness as such are not significant factors in the percentage impairment of speech reception thresholds. Comparison of audiometric and speech reception levels shows that frequencies above and below 512 and 2048 have little significance in the subject's ability to understand speech. A classification of speech reception threshold is presented.

Sabine,[25] writing on the estimation of the percentage loss of hearing, says:

> On the basis of the commonly accepted theory, that the loudness of a tone is proportional to the number of nerve fibers stimulated, it may be said that a given sound received by both ears is twice as loud as the same sound presented to one ear.

24. Hughson, W., and Thompson, E.: Correlation of Hearing Acuity for Speech with Discrete Frequency Audiograms, Arch. Otolaryng. **36**:526-540 (Oct.) 1942.

25. Sabine, P. F.: On Estimating the Percentage Loss of Useful Hearing, Tr. Am. Acad. Ophth. (1941) **46**:179-187 (March-April) 1942.

> The maximum increase in intensity to produce a loudness sensation in one ear equal to that produced, when the same intensity is produced in both ears, is of the order of ten decibels. Experimental data already adducted indicate that complete deafening in one ear . . . will result in a negligible decrease in the intelligibility of speech at conversational level, heard from a point in front of the listener.

Clinical observations indicate that a person having normal hearing in one ear exhibits no difficulty in understanding direct conversation. Obviously, one good ear is as good as two for telephone communication. The foregoing considerations indicate that when both ears are taken into account in evaluating hearing loss, relatively small weight should be given to the loss for the poorer ear. On the other hand, the following facts call for allowance of some weight to loss in that ear.

1. Binaural hearing aids in locating the source of sound and is useful in hearing wanted sounds in the presence of disturbing sounds.

2. The effect of reverberation in a room in decreasing the intelligibility of speech is more pronounced with monaural than with binaural listening.

3. Loss of hearing in one ear increases the possible damage that might result from any possible future injury to the remaining ear.

Accordingly, the author suggests in a purely tentative way that the percentage loss of hearing, for both ears, be computed as follows:

Compute the total loss of hearing for both ears from the percentages assigned in hearing loss chart (fig. 4). To the percentage loss for the better ear add one eighth of the percentage loss for the poorer ear, the sum to be the total percentage loss of hearing as calculated from the audiograms for the two ears.

A tentative standard procedure for evaluating the percentage of useful hearing loss in medicolegal cases has at last been established.[26] The method was prepared by the consultants on hearing aids and audiometers of the Council on Physical Therapy of the American Medical Association and adopted by the Council and by the Section on Laryngology, Otology and Rhinology at the Ninety-Third Annual Session of the American Medical Association in 1942. It was also adopted by the House of Delegates at its annual meeting in Atlantic City, N. J., in June 1942.

The procedure is based on the threshold measurements of acuity of hearing for air-conducted sound by an accepted audiometer. An accompanying hearing loss chart gives the percentage losses corresponding to measured decibel losses in octave intervals. These percentages

26. Tentative Standard Procedure for Evaluating Percentage of Useful Hearing Loss in Medicolegal Cases: Special Report, Arch. Otolaryng. **36**:590-592 (Oct.) 1942

are based on existing data bearing on the relative values of the different portions of the auditory range for intelligibility of direct speech. Computation of the combined hearing loss for the two ears is indicated at the bottom of the chart. The weighted percentage loss shown by the better ear as compared with that shown by the worse ear of 7 to 1 represents the composite judgment of the committee based on both clinical experience and practical considerations. The percentage loss of hearing is the average of the losses for the two ears taken separately weighted in the ratio of 7 to 1. The percentages shown on the accompanying chart were arrived at from quantitative data.

Otologists interested in the anatomy and physiology of the ear should study Lempert's [27] reports. His article describing the fenestra nov-ovalis is on the "must" list for required reading.

Failure of fenestration operations for otosclerosis results from closure of the operative fistula by new bone or by fibrous tissue. This has caused an increasing interest in the fundamental morphologic response which occurs in bone after injury by the use of various instruments. Recently, for example, attempts have been made to determine the histologic changes which take place in the injury of periosteal bone by different instruments. Canfield [28] made defects with sharp and dull instruments in the skull of a cat and concluded that the polishing and burnishing burrs were capable of preventing bone regeneration. The Guggenheims [29] carried out a series of experiments on the skulls of adult white rabbits and created defects by means of sharp and dull instruments. These investigators reported that two months and two days after operation the most patent fistula was that made with a sharp instrument.

Lempert, Meltzer and Spector,[30] to test the validity of such opposing claims, carried out experiments on the skulls of 12 cats, ranging in postoperative age from seven to forty-six days. The following conclusions were arrived at:

1. Given sufficient time, growth of new bone will take place in lesions made with any type of instrumentation; no single instrument

27. Lempert, J.: Fenestra Nov-Ovalis: A New Oval Window for the Improvement of Hearing in Cases of Otosclerosis, Arch. Otolaryng. **34**:880-912 (Nov.) 1941.

28. Canfield, N.: Labyrinthine Fistulas: Report on Experiments on the Vital Response to Various Methods of Producing Defects in Bone, Arch. Otolaryng. **30**:50 (July) 1939.

29. Guggenheim, L. K., and Guggenheim, P.: Artificial Fistula in Otosclerosis, Tr. Am. Laryng., Rhin. & Otol. Soc. **46**:509, 1940; Arch. Otolaryng. **32**:1 (July) 1940.

30. Lempert, J.; Meltzer, P. E., and Spector, B.: Bone Repair Following Defects Made in the Skull of Cats by Means of Different Instruments, Arch. Otolaryng. **36**:473-490 (Oct.) 1942.

used to create a defect in the periosteal bone of the skull of either the cat or the rabbit is capable of inhibiting completely the natural tendency toward bone regeneration.

2. The observations fail to substantiate the conclusions either of Canfield or of the Guggenheims, but the authors suspect that the burnishing and polishing burrs tend to retard and inhibit the osteogenesis, although in none of their experiments did these instruments succeed in entirely preventing new bone regeneration.

3. Their results, as well as those of Canfield and the Guggenheims, cannot without caution be carried over in toto in the interpretation of what takes place in fenestration of the horizontal semicircular canal of the human labyrinth. Though Lempert can point to hundreds of operations on human labyrinths in which the polishing and burnishing burrs were employed to create the fenestra in the external semicircular canal and such fenestrae remained patent because osteogenesis did not take place, he does not believe that the use of these burrs was the sole reason for the failure of bone regeneration to take place in these cases. Further investigation of this problem is now being concluded on the monkey labyrinth.

Van Gilse [31] reported that exostoses in the external auditory canal are often found in cold water swimmers. In a discussion of his paper at the Collegium Otolaryngologicum in Venice in 1937, it was brought out by Italian otologists that exostoses are rarely seen in Italy. The inference is that Italian swimmers, who usually use the warm water of the Adriatic, are not subject to exostosis to the same extent as are the Dutch, who are wont to swim in the cold waters of the North Sea or in the Baltic. Fowler and Osmun [32] found that of 25 patients with hyperostosis and 9 with discrete exostoses of the external auditory canal, all but 4 had been ardent cold water swimmers. The authors therefore wondered if it would be possible to produce exostoses of the external auditory canal experimentally. Surprisingly, the changes produced by cold water in animals were striking not in the external auditory canal but in the middle ear.

Guinea pigs were subjected to monaural irrigation of the external auditory meatus with cold water. In 4 out of 4 animals in which more than one irrigation was made, there was a diffuse production of new bone in the submucosa of the bulla of the middle ear on the experimental side. The formation of new bone was more or less proportional to the

31. Van Gilse, P. H. G.: Des observations ultérieures sur la génèse des exostoses du conduit externe par l'irritation d'eau froid, Acta oto-laryng. **26**:343-352, 1938.

32. Fowler, E. P., and Osmun, P. M.: New Bone Growth Due to Cold Water in the Ears, Arch. Otolaryng. **36**:455-466 (Oct.) 1942.

number of times the cold water was used as a stimulus and to the total elapsed time. There were no changes in the labyrinthine capsule except for slight growth of new bone on the most exposed portion of the promontory. These changes involved only the periosteal bone. In no case was there any clinical evidence to explain the formation of new bone on the basis of infection. The external canal of the experimental ears showed slight fibrosis and hyalinization of the soft tissue and occasionally a small amount of new bone, but in no case was this alteration sufficiently striking, as compared with the control side, to be of certain experimental origin.

Continuing their studies on pupils of the Pennsylvania School for the Deaf, Hughson and associates [33] discuss the mechanism of inheritance of deafness. A thorough survey of the family history, as well as the complete study of the individual child, has been carried out. This analysis reveals, first, that from the history of the onset and the immediate cause of deafness it is possible to differentiate among the pupils (307) of a school for the deaf the children whose deafness is probably inherited and those whose deafness is acquired. The former apparently constituted about 35 per cent of the school population. The deafness is transmitted according to the mendelian pattern, a single recessive gene being involved.

The significance of these observations lies in their contribution to a clarification of the problem of preventing deafness of the type investigated. On the assumption that the inference regarding heredity is entirely correct, it is immediately perceived that, whether or not a history of deafness in the immediate family can be elicited, a person with embryonic deafness will transmit the particular gene to his offspring and the chances that the transmission is manifest in the offspring will depend on the hereditary makeup of the spouse. It will be further realized that the presence of embryonic deafness among the brothers and sisters, even though the subject has good hearing or the acquired type of deafness, is sufficient to arouse suspicion that the person is a carrier for the recessive gene for deafness. If the figures on the prevalence of nonembryonic deafness in the school surveyed are applicable to all schools for the deaf, it appears that in 65 per cent of the population of such schools factors in the environment are in the main responsible for the deafness.

If hereditary, or biologic, deafness may be assumed to have a mutual hereditary background with allergy, the work of Mao [34] may be

33. Hughson, W.; Ciocco, A., and Palmer, C. E.: Studies on Pupils of the Pennsylvania School for the Deaf, Arch. Otolaryng. **35**:871-882 (June) 1942.

34. Mao, C. Y.: Allergy as a Contributing Factor to Biologic Deafness, Arch. Otolaryng. **35**:582-586 (April) 1942.

important. He finds a higher percentage of allergic reactions in deafened children than in children with normal hearing. The total incidence of positive reactions in 535 seriously deafened children examined was 28.5 per cent, while only 2 per cent showed definite clinical manifestations. These figures present an incidence 27.44 per cent higher for the deafened children than for the largest numerical group (937) of children with normal hearing reported. This greater incidence holds true irrespective of age or sex; in other words, it may be regarded as typical for this entire handicapped group.

Biologic deafness has been shown to develop with decreasing frequency from birth to 3 years of age. By biologic deafness is meant an intrauterine arrest or defect in the development of the auditory mechanism. This condition is present or develops shortly after birth. Since this defect implies immaturity of cochlear structure, and hence inability to function, it may be considered final and irreversible. In the case of the pathologically deafened children, with their equally high incidence of allergic manifestations, it may be assumed that the hereditary factor of allergy renders them constitutionally more susceptible to the influence of various contagious and infectious diseases. The evidence for these conclusions is undoubtedly more presumptive than specific.

Fowler [35] emphasizes that "restoration" of the hearing of the deafened person occurs when tinnitus is alleviated. If the "illusion of loudness" can be made to diminish or disappear, tinnitus assumes its true intensity in the consciousness and may then be borne with equanimity. Drugs alone accomplish little, and success with them is due to the physician's personal interest or his psychologic effectiveness. The otologist must do more than merely make the diagnosis of "tinnitus aurium." There are, according to Fowler, two main types of tinnitus, with different origins.

One type of tinnitus, called vibratory tinnitus, produces no illusion because it is in fact a real sound resulting from actual mechanical vibrations. Vibratory tinnitus, if loud enough, can be (and frequently is) heard by the examiner. Conductive deafness will generally favor a louder reception of vibratory tinnitus than nerve deafness because it excludes environmental masking sounds by lowering air conduction, but does not lower the bone conduction. Nerve deafness does not cut down the loud extraneous sounds to the same extent as conduction deafness because of the recruitment phenomenon which is always present with nerve deafness. Vibratory tinnitus usually comes to the ear through the solid and liquid mediums of the tissues rather than through the gaseous elements (the air) and may, therefore, be considered as bone

35. Fowler, E. P.: The "Illusion of Loudness" of Tinnitus—Its Etiology and Treatment, Laryngoscope **52**:275-285 (April) 1942.

conduction tinnitus. The more common types of vibratory head noises arise from contraction of the intratympanic and tubal muscles, extracranial aneurysms, arterial or arteriovenous aneurysmal angiomas, bruits in the jugular bulb or vein, other hemic murmurs, clicks and squeaks about the joints of the jaw, spasms of muscles of the face and neck, bubbles in the eustachian tubes and various sounds from the respiratory and gastrointestinal tracts.

Another type of tinnitus, nonvibratory tinnitus, has no existence outside the sufferer, and no existence within him except as a sensation resembling sound. It originates by local or reflex biochemical irritation, not mechanical vibrations, of the neural elements of the auditory apparatus. Therefore nonvibratory tinnitus is an illusion of sound. Although measurements demonstrate this type of tinnitus to be only 5 to 10 decibels in loudness, patients frequently describe it as very loud, sometimes as deafening and unbearable and as driving the sufferer insane. Peripheral nonvibratory tinnitus may be likened to an irritation (tingling, tickling or itching) of the basilar membrane and its tonal quality to an irritation of particular tonal areas of the membrane. Central nonvibratory tinnitus, on the other hand, may be said to represent a less differentiated, or mass, irritation of neural elements. The tinnitus in cases of such mass irritation shows little resemblance to patterns obtained from the reception of actual sound, except those from mass stimulations, such as thermal noise. The symptoms are due to the rhythmic and more or less synchronized firings of neural elements irritated by pressure, destruction or other biochemical irritations, in the same way that other nerves of sensation may be activated under comparable circumstances. The type of deafness associated with nonvibratory tinnitus is always nerve deafness, no matter what other types may be superimposed. The location of origin of nonvibratory tinnitus may usually be determined by its tonal and masking characteristics in relation to the threshold and recruitment of loudness measurements. Nonvibratory tinnitus is associated with many disorders. It is a part of the so-called Ménière syndrome. Acoustic shock or other trauma to the inner ear, intracranial arteriosclerotic lesions, aneurysm, brain tumor, pressure, anoxia, change in p_H, allergic disorders and disturbances in water balance and toxic, degenerative or regenerative biochemical irritations of the auditory nerves may all cause nonvibratory tinnitus. Drugs, poisons and many diseases may also act as irritants.

It depends on the character and place of origin of the tinnitus whether therapeutic measures increase, diminish or fail to influence it. Taterka [36] reports that prostigmine methylsulfate is of definite value in the treat-

36. Taterka, H. D.: Preliminary Study of the Effect of Prostinmin on Tinnitus, Laryngoscope **52**:299-302 (April) 1942.

ment of tinnitus, 12 out of 21 patients being improved. Schluederberg [37] noted improvement in 10 out of 30 patients with tinnitus after such treatment. Fowler,[38] on the other hand, thinks the drug is of little value in the treatment of tinnitus and deafness, observing that subcutaneous injections of saline solution gave almost as high a percentage of improvement.

VESTIBULAR PHYSIOLOGY

A mathematical study of the effects of various types of motion on differences in hydrostatic pressure between ends of a semicircular canal is presented by Morgan, Summers and Reimann.[39] In this paper a semicircular canal has been idealized by making the following assumptions: 1. There is no flow of endolymph in the canal. 2. Response to motion is due to pressure changes produced at the ends of the canal. 3. The walls of the canal are rigid. 4. The endolymph is incompressible and fills the entire canal. The mathematical analysis for every possible type of motion that shows pressure differences between the ends of the canal are produced only by linear acceleration or by angular acceleration or velocity about axes oriented in specific ways in respect to the canal. The pressure differences thus arising in the canal may be presumed to be a source of nerve stimuli. The mathematical expressions for differences in hydrostatic pressure produced by the various motions are quite simple and would lend themselves readily to experimental verification. Thus evidence could be obtained to determine whether or not there is an endolymphatic flow in the production of nerve stimuli in the semicircular canal.

Nystagmus is studied by Arellano,[40] who presents new information on the kinetovisual function of the vestibular apparatus and on kinetic vision. The mechanism of vision when the head and external objects are still is well known. During rotatory movements of the head objects appear to turn around in the same plane but in the opposite direction. Owing to stimulation of the semicircular canal apparatus nystagmus develops. Fixation of gaze, unless prevented by Bartel's lenses, can prevent the development of nystagmus even with rapid rotation. The nystagmus turns around the axis of rotation of the head, with its slow component in an opposite direction and its rapid component in the

37. Schluederberg, H.: Treatment of Deafness and Tinnitus Aurium with Prostigmin, Ann. Otol., Rhin. & Laryng. **51**:526-530 (June) 1942.

38. Fowler, E. P.: Nonsurgical Treatment for Deafness, Laryngoscope **52**: 204-217 (March) 1942.

39. Morgan, R.; Summers, R. D., and Reimann, S. P.: Effects of Various Types of Motion on Differences in Hydrostatic Pressure Between Ends of a Semicircular Canal, Arch. Otolaryng. **36**:690-703 (Nov.) 1942.

40. Arellano, E. R.: Vestibular Kinetovisual Function and Kinetic Vision, Arch. Otolaryng. **36**:95-107 (July) 1942.

same direction. This reaction is due to stimulation of the semicircular canal apparatus.

Each time the eye follows a sector of the panorama, impelled by the slow component, the eye and the panorama are displaced in the same direction, and the optical image of that sector of the panorama remains stationary on the retina, and thus the retina may be stimulated in such a manner as to produce normal visual perception. Each time the eye is directed to the next sector of the panorama by virtue of the rapid component, the optical object will move rapidly on the retina, with a speed equal to the sum of the velocities of the two manifestations, owing to the fact that the eyes and the panorama move in opposite directions. On account of the swiftness of the displacement of the optical image, stimulation will not occur and no visual perception will be produced. Vision cannot take place during movement of the head if nystagmus is absent.

Compensatory movement around the transverse axis of the head (vertical plane) is observed when the head is inclined forward or backward. The compensatory movements of the eyes are produced by stimulation of the otolithic apparatus. It is supposed that when the vertical axis of the head is inclined, gravitation produces a displacement of the otoliths which modifies the pressure or the tension exerted by the otoliths on their respective maculas, with resultant stimulation of the macular endings of the vestibular nerve in this apparatus. The eye turns slowly around the axis and in the direction opposite that of the inclination of the head. Thus the optical image of the panorama which would slide over the retina if the eye were stationary during the inclination of the head will now remain fixed in the retina because the eye and the panorama are moving in a similar manner.

The action of the vestibular apparatus in kinetic vision may be compared to that of an eye stabilizer, serving to keep the eyes in the same position or orientation with relation to the panorama during the movements of the head, in order to maintain the optical images centered on the retinas while stimulation is effected. When the movement of the optical image of external objects is due to any cause other than a movement of the head, the retinal reflexes move the eyes in the same manner as the objects move. Thus kinetic vision is based on the same mechanical principles that are used in cinematography; that is, one obtains the vision of moving objects by means of a series of still pictures.

The exact cause of Ménière's disease is not known. Furstenberg and associates [41] in 1934, prompted by visionary speculation and in the

41. Furstenberg, A. C.; Lashmet, F. H., and Lathrop, F. D.: Ménière's Syndrome Complex: Medical Treatment, Ann. Otol., Rhin. & Laryng. **43**:1035-1047 (Dec.) 1934.

hope that a theory might be reduced to facts, undertook studies of water balance on patients with this disease. They suggested the possibility of cerebral hydration or waterlogging as the responsible etiologic factor in Ménière's disease, and the theory furnished the concept that the removal of body fluids, or dehydration, might eliminate the offending influence and restore the patient to normal equilibrium. They found that the quantity of water in the patient's tissue at any given time bore no relation to Ménière's disease but that sodium used in hydrating the patient appeared to initiate the characteristic vertiginous attacks of this disorder. It seemed that the tissues responsible for Ménière's disease were sensitized to or had an increased avidity for the sodium ion. The treatment, therefore, was to prescribe a sodium-free diet and to insure the maximum elimination of sodium by the administration of the acid-forming salt ammonium chloride.

Furstenberg and associates [42] treated 100 patients suffering from Ménière's disease by this method, with uniformly satisfactory results. The authors have been unable to substantiate by laboratory experimentation the original premise that the sodium ion is the offending influence in the production of the vertiginous attacks of Ménière's disease; neither have they been able to disprove this theory. Attempts to determine the sodium content of the blood of patients with Ménière's disease have not met with encouraging results. It need not be assumed that if there is retention of sodium in the otic labyrinth, this is reflected in the sodium content of the blood. Indeed, the sodium content of the blood is not elevated in Ménière's disease. In Addison's disease the sodium content of the blood may be within normal limits; yet the cortex of the adrenal gland, which is said to control the metabolism of sodium, is extensively damaged. It is reasonable to assume that the slight retention of sodium which occurs perhaps in the labyrinth of a patient suffering from Ménière's disease is not necessarily associated with a similar retention of this ion in the blood.

The present paper is based on the follow-up study of 35 patients with the typical signs and symptoms of Ménière's disease. The average duration of treatment of this group was thirty-two months, the minimum being three months and the maximum seven years. The ages were from 16 to 67 years, but most of the patients were adults in the fifth or sixth decade of life (average age, 49 years). The group was strikingly free from any physical evidence of disease, and all of them were reported in excellent health except for the symptoms for which they were seeking relief. Every patient was hospitalized for seven to ten days when the treatment was first instituted, in order to acquaint him with the proper

42. Furstenberg, A. C.; Richardson, G., and Lathrop, F. D.: Arch. Otolaryng. **34**:1083-1100 (Dec.) 1941.

diet and to facilitate a thorough examination. The authors stress the importance of hospitalization. All their patients were given a low sodium, neutral diet and large doses of ammonium chloride (3 Gm. in capsule form three times daily with meals for three days, then none for two days).

Strict observance of the full regimen for six weeks is recommended, after which the patient may discontinue the ingestion of ammonium chloride if he has remained asymptomatic. He continues with the salt-free diet for another six weeks; if he is then symptom free he is allowed a small amount of sodium chloride in his cooked food but is warned not to take foods highly seasoned with salt or to use any free salt at the table. If, however, he experiences a return of symptoms, he must revert immediately to the complete therapeutic program. Ammonium chloride in these large doses (18 capsules of 7½ grains [4.88 Gm.] daily) may be administered for an indefinite time without injurious effects.

In this group of 35 patients the average duration of symptoms prior to the institution of treatment was twenty-seven months. The results show that 29, or 83 per cent, of the patients obtained relief from the vertigo. In 51 per cent tinnitus was decreased, and deafness improved in 9 per cent.

The authors say that it would be impossible to explain satisfactorily the absence of vertiginous attacks in this group on the basis of spontaneous remissions, for the reason that they frequently observe the prompt recurrence of vertigo when the patient has become careless about the prescribed diet or when he has attempted to abandon it. Moreover, the prompt disappearance of symptoms with the institution of treatment has been so striking in many patients that it would not be logical to assume that a remission could be so specifically timed.

An addendum contains the specific diets employed, as well as the dosage of ammonium chloride.

Lindsay [43] records the pathologic changes in the inner ear in a case of idiopathic bilateral labyrinthine dropsy (hydrops labyrinthi) with severe deafness. From other reported cases it is apparent that labyrinthine dropsy constitutes a pathologic entity which may produce either auditory disturbances alone or the clinical syndrome known as Ménière's disease. The histopathologic changes in this case provide evidence to explain the interference with function. The functional disturbances cannot be explained on the basis of increased endolymphatic pressure because of the existing mechanism to preserve pressure equilibrium with the perilymph and cerebrospinal fluid. The auditory disturbances

43. Lindsay, J. R.: Labyrinthine Dropsy and Ménière's Disease, Arch. Otolaryng. **35**:853-867 (June) 1942.

characteristic of this disease appear to be most adequately explained on a mechanical or physical basis. The distortion of the saccula and Reissner's membrane and the resulting disproportion of the scala media and the scala vestibuli, along with the relatively well preserved nerve apparatus, suggest an interference with sound transmission in the column of fluid in the cochlea, as in the case of disturbed auditory function. The disturbance of vestibular function and the attacks of vertigo are explained on a physical basis by the occurrence of herniations from the utricle which invade the canals and produce distortion of the walls of the ampullas. Distortion of the ampulla interferes with normal function of the cupula ampullaris and explains both the attacks of vertigo and the depression of caloric excitability in the later stages of the disease. The histopathologic picture explains the favorable effect of certain types of treatment but fails to permit any conclusion as to the pathogenesis. Neither has clinical observation provided any definite indication of the etiologic factors in this type of disease of the inner ear.

Atkinson [44] maintains that histamine should not be used indiscriminately in the treatment of Ménière's syndrome. In about one fourth of all cases of Ménière's syndrome histamine gives a positive cutaneous reaction. Histamine is an irritating substance and produces considerable reaction even in normal subjects. Great care is necessary in interpretation of the reactions. If the patient shows a positive cutaneous reaction the results of desensitization are eminently satisfactory. A second, much larger, group which shows a normal cutaneous reaction to histamine cannot be treated satisfactorily with this drug, except over a short period, virtually the time of an acute attack.

Histamine is well known as a powerful peripheral vasodilator. When used repeatedly it appears to induce in the body an immunity to its action, so that ultimately it loses its dilator effect. It may even cause increased frequency and severity of attacks, and sometimes an increase in deafness. Nicotinic acid is free from this objection and can be given over long periods, with often rapid diminution in severity of attacks. Three illustrative cases are reported in which histamine failed and nicotinic acid succeeded.

395 Commonwealth Avenue.

44. Atkinson, M.: Histamine in the Treatment of Ménière's Syndrome, J. A. M. A. **119**:4-7 (May 2) 1942.

Abstracts from Current Literature

Ear

CEREBELLAR ABSCESSES OF OTITIC ORIGIN IN NINE CHILDREN. FREDERICK SCHREIBER, Ann. Surg. **114**:330 (Sept.) 1941.

The author abstracted briefly 9 cases of cerebellar abscesses in children treated surgically by him. In each instance the symptoms became manifest after mastoiditis and mastoidectomy. The principal diagnostic and localizing signs were atonia and ataxia of the arm on the same side as the abscess. Operation was delayed as long as possible without jeopardizing life from increased intracranial pressure.

BANTIN, Omaha [AM. J. DIS. CHILD.].

ACUTE CATARRHAL MASTOIDITIS. CLAUDE C. CODY, Texas State J. Med. **37**:233 (July) 1941.

Cody reports 4 cases of acute catarrhal mastoiditis, which number he believes is sufficient to establish a clinical entity with a syndrome capable of being differentiated from other otologic diseases, a distinctive roentgenogram, a characteristic pathologic picture at operation and a rational therapy.

The disease is a complication of acute catarrhal otitis media. The patient complains of a "stopped-up" or "stuffy" ear. The symptoms are impaired hearing and, later, tinnitus. There is no pain, fever or secretion in the middle ear.

In Cody's series, the patients were given the routine treatment for acute catarrhal otitis media but did not improve. Incision of the drum membrane was followed by a discharge of moderately thick, canary yellow fluid into the external canal. The discharge ceased after three or four days, with closure of the incision. Repeated incisions and various therapeutic measures failed to improve the condition. Tinnitus increased. There was no fever, no pain or headache about the ear or mastoid, no edema of the superior or posterior walls of the canal and no tenderness or edema over the mastoid. The blood count was normal. Roentgenograms of the mastoid region made more than thirty days after the onset of symptoms showed involvement of the entire mastoid bone but no breaking down of the cell walls.

The pathologic changes observed at operation were those of acute catarrhal inflammation. There was no evidence of bone absorption. The mucous membrane was thickened, and the cells were filled with a thin yellow secretion. The indications for operation were a persistent aural discharge, involvement of the mastoid, as shown by the roentgenogram, progressively increasing deafness of the obstructive type and tinnitus.

Cody states: "Simple mastoidectomy removes the pathologic condition, usually improves the hearing, relieves the tinnitus and probably prevents the later development of either chronic catarrhal otitis media or otosclerosis."

SINGLETON, Dallas, Texas.

HERPES ZOSTER OTICUS TREATED WITH OMNADIN. F. U. MAGNUSSEN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **47**:119 (Dec.) 1940.

Magnussen reported a case of herpes zoster oticus which was characterized by the usual syndrome of pain, herpes, deafness and paralysis of the face. The patient was given 2 cc. of omnadin (a sterile solution of protein substances obtained from nonpathogenic bacteria [Sarcina and Bacillus mycoides], various animal fats and lipoids derived from bile) intramuscularly on the first, second and fifth days

after admission to the hospital. After the first injection she showed decided improvement in her facial paralysis, and on the fifth day after her admission hearing was spontaneously restored. There were no recurrences, and she was discharged, completely cured.

PERSKY, Philadelphia.

DIAGNOSTIC SIGNIFICANCE OF THE AUDIOGRAM IN CASES OF IMPAIRED HEARING. LUDWIG STERN, Ztschr. f. Hals-, Nasen- u. Ohren. **47**:150 (Dec.) 1940.

Stern, in evaluating the significance of the various curves of a series of audiograms, attempted to establish a typical curve as a diagnostic index to the different types of hearing impairment. He classified the types of hearing loss as: (1) conductive impairment, with changes in the tympanic membrane; (2) otosclerosis; (3) deafness arising in the internal ear; (4) mixed deafness; (5) central deafness, and (6) deafness due to injuries to the skull. He found that there was a close parallelism between the audiometric features and the clinical diagnosis and that there did not appear to be a frank contradiction in a single case. The audiogram had particular significance in cases of otosclerosis.

A comparison of the audiogram and the results of the spoken voice tests also showed a close similarity, except in cases of internal ear deafness, in which the spoken voice test showed a variance. It is with this type of hearing impairment that the audiogram is of signal importance, since it can often detect an early alteration of hearing acuity. The author finally discussed the significance of the high tone (c-5) dip, which is present in many audiograms. This may be isolated either in a pathologic or in an apparently normal ear. This dip suggests early involvement of the inner ear. This cochlear degeneration may have a hereditary, an idiopathic, a toxic or a traumatic source. If traumatic, it is likely to be due to an acoustic rather than a mechanical form of trauma.

PERSKY, Philadelphia.

SIGNIFICANCE OF CELLS OF THE PETROUS PYRAMID IN OTITIS MEDIA. BERNHARD LANGENBECK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **47**:339 (Feb.) 1941.

In discussing the pneumatization of the petrous pyramid, Langenbeck describes two types: the first, in which the cells extend to the very tip of the pyramid, and the second, in which the cells extend only to the plane of the superior semicircular canal. In the latter type, called the perilabyrinthine, cells may extend above, behind or below, but never beyond, the internal auditory meatus. Owing to divergence in the clinical course of infection of the petrous process, the uncertainty of indications for operative procedure and the relation to otitis media, a careful evaluation of these two types is necessary. Furthermore, Langenbeck found that roentgenographic examination was of real value when the infection involved the cells of the petrous tip, but was inconclusive when it was confined to the perilabyrinthine region.

The author believes that involvement of the perilabyrinthine cells per se is only a mild clinical complication, the management of which is easily effected by thorough mastoidectomy. In most cases even an extension of the infection into the petrous tip does not seriously influence the clinical course of the disease (provided free drainage is maintained). The need for direct operative intervention in involvement of both types of cells is relatively small. Usually, the cure occurs either spontaneously or after mastoidectomy. The real importance of the problem rests on early diagnosis of this complication and a subsequently early mastoidectomy, to afford a greater opportunity for an earlier avenue of drainage of any of the infected areas.

PERSKY, Philadelphia.

EFFECT OF NOISE ON NORMAL AND IMPAIRED HEARING. P. WEERSMA, Ztschr. f. Hals-, Nasen- u. Ohren. **47**:402 (Feb.) 1941.

Weersma studied the masking effect in audiometry. This is an important aid, but its use must be understood. If the tone to be masked is lower than the masking tone, the effect of the latter is negligible. If the two tones are relatively close,

the masking action is most effective. Finally, if the masking tone is lower than that tested, the results have no significance.

The author constructed a special instrument which would produce a masking effect at different frequencies. He found that the audiogram of both normal and impaired hearing presented a new form of curve, with "dips" that were frequently missed by the usual method of examination. PERSKY, Philadelphia.

Larynx

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEOESOPHAGEAL FISTULA: REPORT OF A SUCCESSFUL EXTRAPLEURAL LIGATION OF FISTULOUS COMMUNICATION AND CERVICAL ESOPHAGOSTOMY. N. LOGAN LEVEN, J. Thoracic Surg. **10**:648 (Aug.) 1941.

The author reports the surgical treatment of congenital atresia of the esophagus with tracheoesophageal fistula in an infant, who at the time of publication of the report had reached the age of 1 year and 7 days. He discusses the previous attempts at correction of this deformity, all of which have met with uniformly unsuccessful results at the hands of the most competent surgeons. From previous experience with gastrostomy in the care of infants with such anomalies the author decided that direct attack on the fistulous communication is necessary.

After careful preparation, the infant was gastrostomized, and between this procedure and the next a catheter was kept leading into the jejunum through the pylorus. The mouth was frequently aspirated of mucus. Through an extrapleural approach with resection of the right fourth rib, the fistulous communication between the trachea and the esophagus was doubly ligated with silk, after the azygos vein had been ligated and divided. Two and one-half months later, the blind proximal pouch of esophagus was brought out through a left cervical incision. This was connected with the gastrostomy opening. An antethoracic esophagoplasty is contemplated for the future to reestablish continuity. This is a remarkable case report. DORSEY, Chicago [AM. J. DIS. CHILD.].

THE OPEN SAFETY PIN. LYMAN G. RICHARDS, New England J. Med. **225**:561 (Oct. 9) 1941.

This interesting article, which is primarily concerned with the possible locations, positions and detailed methods of removal of open safety pins from the hypopharynx (above the cricopharyngeal ring), various portions of the esophagus, larynx, trachea and bronchi, has also some helpful suggestions to the pediatrician. The most important is to educate mothers, nurses and nursemaids always to close safety pins after their removal from the clothing of infants and children and in any case to place them well out of their reach.

The second suggestion is that whenever an infant or child suddenly chokes, coughs and perhaps vomits, the swallowing or aspiration of a foreign body should be suspected, and if a pin, metal clasp or other metallic object is missing a diagnostic roentgenogram should be made.

As a third point the author states that it is in the hypopharynx, particularly in infants up to the age of 1 year, that one finds over 50 per cent of all open safety pins.

Fourth, the warning is given that only in a life-saving emergency should the general practitioner or pediatrician attempt the removal of an open safety pin, as the procedure usually requires the aid of a well trained and experienced bronchoscopist. GENGENBACH, Denver [AM. J. DIS. CHILD.].

TRACHEOBRONCHITIS COMPLICATING GRIP AND ITS TREATMENT. HANS LEICHER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **47**:111 (Dec.) 1940.

The author discusses tracheobronchitis as a complication of grip and differentiates three stages: (*a*) simple tracheobronchitis, characterized by redness and swelling of the mucous membrane, with moderate mucoid secretion; (*b*) hemor-

rhagic tracheobronchitis, characterized by punctate hemorrhages throughout the mucous membrane, but without any interference with respiration, and (*c*) obstructive dry hemorrhagic tracheobronchitis. There are no pathognomonic features in the second stage, and consequently a differential diagnosis from measles and scarlet fever is difficult.

Of a series of 510 cases, Leicher was able to make a direct tracheoscopic examination in 260. Seventy-one per cent of his cases represented the first stage, 29 per cent the second stage and only 2 cases the third stage.

He discusses the last 2 cases in detail. In 1 case he performed tracheotomy and inserted a tube, through which he removed the thick crusts that obstructed the airways, while in the second case he was able to remove the obstructing masses through a tracheoscope. Both patients recovered, but he stressed the seriousness of this complication, the gravity of the prognosis and the high mortality, death being usually due to bronchopneumonia.

PERSKY, Philadelphia.

Nose

CANCER OF PARANASAL SINUSES. WILLIAM L. WATSON, Laryngoscope **52**:22 (Jan.) 1942.

Watson analyzed 127 cases of primary cancer originating in one or another of the paranasal sinuses to determine a pattern of this disease. He used the consecutive series of patients admitted to the Memorial Hospital for the Treatment of Cancer and Allied Diseases, in New York, during the ten year period between 1928 and 1938. The admission incidence was 0.44 per cent of the total admissions, indicating that cancer primary in the paranasal sinuses is a comparatively rare disease. Cancer occurred in the maxillary antrum more frequently than in all the other sinuses combined (105 to 22 cases); the ethmoid sinus was the next most frequently involved (7 cases). The age distribution was conventional except that 4 patients in the series were under 15 years of age and there was none between the ages of 14 and 27. Sinal cancer became well established before symptoms called attention to the disease. The first symptoms, in order of frequency, were pain, swelling of the cheek, nasal obstruction and nasal bleeding. Stereoscopic roentgenograms were diagnostic for 83 per cent of the patients studied, showing invasion or actual destruction of bone. Where no ulceration was visible, aspiration biopsy was of utmost value in differentiating between a benign and a malignant process. Aspiration biopsy established the preoperative diagnosis in 39 instances, and a negative report was obtained in 4 cases. Eighty-nine per cent of the cancers proved to be of the squamous or epidermoid type with 60 per cent of these in the grade 2 group. Metastasis occurred in 29 per cent of the series. Treatment combined surgical procedures with interstitial radon therapy and roentgenotherapy. Forty-five patients were operated on without an operative death. The most frequent complication was osteoradionecrosis followed closely by cellulitis and panophthalmitis. Twenty and five-tenths per cent of a determinate group were "cured" of their cancer or at least had the process arrested.

WOOD, Newark, N. J.

TERTIARY SYPHILIDS OF THE NOSE. JAMES S. SNOW, South. M. J. **34**:713 (July) 1941.

The author reports on a study of a series of 42 cases of late syphilids of the nose. Acquired syphilis occurred in 40 cases; in the other 2 cases the disease was due to congenital infection. In the series there were 31 females and 11 males—a ratio of almost 3:1.

The clinical picture is described, and the differential diagnosis is discussed in detail. The author states that in making a diagnosis late syphilids of the nose must be differentiated from such conditions as tuberculosis cutis, epithelioma, rosacea-like lesions, infectious eczematoid dermatitis, impetigo, ringworm, bromoderma, ioderma, blastomycosis, leprosy, rhinoscleroma and glanders.

Before antisyphilitic treatment is started, it is necessary to secure a complete physical examination, especially in regard to the cardiovascular, hepatic and central nervous systems. The treatment should be adapted to the individual patient; otherwise serious or fatal complications may be precipitated by the therapy. With proper and adequate antisyphilitic treatment, the cosmetic results in these cases were surprisingly good.

SINGLETON, Dallas, Texas.

CONGENITAL ATRESIA OF THE POSTERIOR CHOANAE OF THE NASAL FOSSAE. J. A. LUMSDEN-COOK, South African M. J. **15**:498 (Dec. 27) 1941.

The author reports 2 cases of congenital atresia of the nasal choanae, in 1 of which the condition was bilateral and in the other unilateral. The condition may be due to persistence of the nasopharyngeal membrane, persistence of the buccopharyngeal membrane or overgrowth of the horizontal and vertical processes of the maxilla. In complete bilateral atresia the symptoms are usually most urgent, as the child has a natural tendency to keep the mouth closed and to breathe through the nose. Thus the child may die of asphyxia before the condition is realized, or milk may be inspired into the lungs, causing bronchopneumonia. On the other hand, unilateral atresia may go unrecognized for a considerable time and the patient be subjected to repeated curettage for adenoids before suspicion is aroused. The outstanding symptoms are tendency to asphyxia, difficulty in sucking, mouth breathing, inability to pass a probe through the nose and lack of movement of the muscles of the alae nasi. In unilateral atresia these symptoms are not so pronounced, as the child is able to breathe through the patent nostril. As the infant grows older, a tendency for mucus to accumulate on the affected side will be noted. There is a continuous ooze from the nose. Infection may spread to the antrums. The nasal mucous membrane may undergo atrophic degeneration, leading to ozena. The affected side of the face fails to develop equally with the other side, and in addition some of the paranasal sinuses may remain solid. The general physique is poor, but a striking improvement takes place after the obstruction is removed. The operative technic used for correction of the condition is described.

GONCE JR., Madison, Wis. [AM. J. DIS. CHILD.].

Miscellaneous

LUMBAR PUNCTURE AS A FACTOR IN THE PATHOGENESIS OF MENINGITIS. LAURENCE G. PRAY, Am. J. Dis. Child. **62**:295 (Aug.) 1941.

Pray reviews the pathogenesis of meningitis and suggests that it arises in one of three general ways: Organisms may reach the subarachnoid space by direct traumatic implantation; infection may extend to the meninges from an adjacent lesion, or organisms may reach the meninges by passing the blood-brain barrier. Because lumbar puncture entails the risk of producing meningitis, he considers it important to determine the degree of risk. For this purpose he selected 207 cases of pneumococcic meningitis. Lumbar puncture was done before the onset of meningitis in 13, or 6 per cent, of these. As a result of his studies Pray feels that although the conclusions from experimental work make it obvious that lumbar puncture may be an important factor in the production of meningitis in cases of bacteremia, it was not an important factor in the clinical cases which constituted his material of study. Lowering of cerebrospinal fluid pressure may produce meningitis not only by drawing organisms through the blood-brain barrier but by making possible a rupture into the subarachnoid space of a focus of infection contiguous with the meninges, through release of pressure. Lumbar puncture made through infected tissues may introduce organisms directly into the meninges. In spite of these risks, the necessity of arriving at a diagnosis is frequently sufficiently important to warrant making the puncture. Pray concludes that the material which he studied is evidence that, in general, lumbar puncture is not hazardous for the patient with bacteremia, and he bases this conclusion on the

fact that the incidence of meningitis was no greater among patients with bacteremia who had lumbar puncture with a yield of normal spinal fluid than among those for whom no diagnostic tap was performed. In general, he minimizes the danger of producing meningitis by the diagnostic spinal tap.

WAGGONER, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

THE USE OF RABBIT THROMBIN AS A LOCAL HEMOSTATIC. E. L. LOZNER, H. MACDONALD, M. FINLAND and F. H. L. TAYLOR, Am. J. M. Sc. **202**:593 (Oct.) 1941.

The authors report early clinical observations on the use of rabbit thrombin as a local hemostatic agent. Thrombin precipitates fibrin instantaneously, independently of any other factors in the blood coagulation reaction. This has hitherto not been of marked clinical importance because of the difficulty in preparation of the thrombin. Increased availability has now been achieved by the isolation from rabbit plasma by Parfentjev of a globulin fraction possessing great activity.

A controlled study of hemostasis in normal subjects utilizing a standard trauma revealed that the most effective method of treatment was the direct application to the wound of a square of filter paper (or gauze) dampened with saline solution and sprinkled with dry thrombin. A solution of rabbit thrombin used similarly or the dry powder used in a spray was also effective. Observations were then carried out on 11 patients bleeding from small wounds, of whom 9 had hemorrhagic diatheses and 2 had hypertension with epistaxis. Altogether, 4 patients with epistaxis were treated, 1 of whom with hypertension had had persistent bleeding for fourteen days prior to rabbit thrombin therapy despite the use of various hemostatics and four blood transfusions. The dry powder was employed for the majority of patients and was thought the most effective, although it was felt that the solution of rabbit thrombin was also of value. In 10 patients the hemostasis produced was complete and immediate; in the remaining case the hemostasis was, on the first application of rabbit thrombin, only partial, but two subsequent applications on following days produced complete and immediate hemostasis, and it was thought that the partial failure was due to faulty technic. (NOTE: The abstracter has had the opportunity of using the rabbit globulin prepared by Parfentjev in a case of persistent serious epistaxis associated with fractures of the maxilla which involved the floor of the nose. The bleeding had not been checked by packing with strips of gauze impregnated with various hemostatics, including epinephrine, hydrogen peroxide and cocaine, for several hours, but responded quickly to the rabbit globulin used similarly.)

JENNES, Waterbury, Conn.

CAROTID SINUS SYNDROME. MARVIN F. JONES and JOHN M. CONVERSE, Ann. Otol., Rhin. & Laryng. **50**:806 (Sept.) 1941.

The anatomy, physiology and clinical pathology of the carotid sinus syndrome are discussed. The symptoms are typical: The patient feels weak, then faint; he has an intense feeling of dizziness, often a sensation of a vacuum on that side of the head, and then loses consciousness. In milder forms syncope is not complete and the patient merely feels faint or dizzy. Three forms are recognized: the vagal, the depressor and the cerebral type. Symptoms may appear without any apparent cause; they may appear after an emotional upset or mechanical stimulation by a tight collar or may be caused by pressure of overlying hypertrophied lymph nodes or a tumor, an aneurysm of the carotid artery, or a hypertrophic sternocleidomastoid muscle. Certain drugs, such as digitalis, have a sensitizing effect, and their use before administration of a general anesthetic should be discouraged. In the presence of unexplained attacks of syncope, the carotid sinus syndrome should be considered. A clinical diagnostic test is the production of total loss of consciousness, faintness or dizziness by pressure over the area of the carotid sinus.

Blocking the area with procaine hydrochloride is another method. Conservative treatment should be used with the milder forms, but if the attacks are frequent and alarming to the patient or his family and medical treatment is unsatisfactory, surgical intervention is indicated. M. V. MILLER, Philadelphia.

SOME DENTAL OBSERVATIONS BY AN OTOLARYNGOLOGIST. GORDON BERRY, Ann. Otol., Rhin. & Laryng. **50**:995 (Dec.) 1941.

Berry feels that the otolaryngologist should take more interest in the dental problems of his patient. He reviews anomalies of development of the palatal arch, abnormalities of eruption and impactions of teeth, faulty bite and the resulting effect. He briefly discusses dental infection and diagnosis by transillumination, and infections of the upper and lower jaw secondary to dental involvement. Infection of the maxillary sinus of dental origin is discussed together with the problem of a dead tooth beneath the antrum when the roentgenogram fails to show dental infection. M. V. MILLER, Philadelphia.

ABSORPTION OF QUININE INTO THE CEREBROSPINAL FLUID OF THE FETUS IN UTERO. H. MARSHALL TAYLOR, LUCIEN Y. DYRENFORTH and CASH B. POLLARD, Ann. Otol., Rhin. & Laryng. **50**:1030 (Dec.) 1941.

That quinine is an etiologic factor in deafness of the newborn is an accepted fact. Because of the wide use of quinine generally in the treatment of diseases concurrent with pregnancy and its use in induction of labor, the authors conducted some research into the presence of the drug in the circulating cerebrospinal fluid. The quinine was detected in the cerebrospinal fluid and urine of 7 infants delivered of mothers who had received oxytocic doses of quinine bisulfate, and the clinical and chemical procedures are given. The authors feel that their results give important evidence that the drug should be used with caution in diseases concurrent with pregnancy and that its indiscriminate use as an oxytocic drug may have a malignant influence on the fetal ear. M. V. MILLER, Philadelphia.

TREATMENT OF PNEUMOCOCCIC MENINGITIS. C. W. STEELE and J. GOTTLIEB, Arch. Int. Med. **68**:211 (Aug.) 1941.

Steele and Gottlieb present evidence which suggests that the abandonment of sulfanilamide and its derivatives in the treatment of pneumococcic meningitis may have been erroneous. They state that of 48 patients treated with sulfanilamide and its derivatives 68.75 per cent (33) recovered and 31.25 per cent (15) died, whereas of 67 similar patients treated with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) only 53.7 per cent (36) recovered and 46.2 per cent (31) died. If all patients who died during the first twenty-four hours are excluded, the respective percentages of recoveries become 71 and 62.7. Sulfapyridine was more effective than sulfanilamide and its derivatives for type III pneumococcic meningitis. Administration of type-specific antipneumococcus serum in conjunction with chemotherapy did not materially lower the mortality. As sulfanilamide is a safer drug, is more readily and uniformly absorbed and is as effective as or even more effective than sulfapyridine or sodium sulfapyridine for pneumococcic meningitis, its use should be continued until either of the other two drugs is shown to be superior. J. A. M. A.

CONCENTRATION METHOD OF RADIOTHERAPY FOR CANCER OF THE MOUTH, PHARYNX AND LARYNX. MAX CUTLER, J. A. M. A. **117**:1607 (Nov. 8) 1941.

The author presents the results of his recent efforts to influence the more radioresistant forms of cancer of the mouth, pharynx and larynx by means of new methods of roentgen ray and radium treatments. The study is based on

observations on some 850 patients with cancer of the mouth, pharynx and larynx treated in the Chicago Tumor Institute and the Hines Veterans Hospital.

He describes in some detail the important points connected with the "Coutard method" and the technics used and credits much of the inspiration for his ideas to Coutard. Radiosensitivity, clinicopathologic classification in relation to radiosensitivity and efforts to sterilize the radioresistant lesions are fully discussed.

Next, he reports in full detail his method of concentration, the basis of which consists in the use of large daily doses over a short treatment period (nine to twelve days), the total dose being sufficient to produce *epithélite* and *epidermite*. In selected cases the daily dose is increased as the size of the port is diminished. He outlines the specifications concerned with voltage, intensity, fields, time, daily and total doses, etc.

This method of concentration has been used only three and one-half years, so that the permanence of the results cannot as yet be accepted; yet the method has given results in some cases of carcinoma of the mouth, pharynx and larynx which failed to respond to all other methods of external irradiation.

The "method of concentration" has the following basis: The conception that the more radioresistant forms of cancer require a higher daily dose and a shorter total treatment period (twelve days or less); the administration, in selected cases, of an increasing daily dose through a diminishing port in order that the central, more radioresistant, portion of the lesion may receive a much larger dose than is possible when the size of the port remains constant; the administration of the classic *epidermite* and *epithélite* dose, such dose representing the maximum treatment that can be tolerated by the normal tissues of the tumor bed. The interrupted method of irradiation has proved especially satisfactory.

GORDON, Philadelphia.

THE IMPORTANCE OF AIR-BORNE PATHOGENIC BACTERIA IN THE OPERATING ROOM: A METHOD OF CONTROL BY STERILIZATION OF THE AIR WITH ULTRAVIOLET RADIATION. DERYL HART, J. A. M. A. **117**:1610 (Nov. 8) 1941.

The author has carried out extensive studies to determine the cause of "unexplained infections" in clean wounds and, after some five and one-half years in the operating rooms of Duke Hospital, concludes that the pathogenic bacteria floating in the air and falling on the wound and sterile field may be the answer to his search. After a minute analysis of all factors dealing with the "aseptic technic" in the operating room, he set out to deal with the air-borne pathogenic bacteria as thoroughly as possible. The details are fully covered in the text, and his conclusions are as follows:

"It is felt that the air contaminated by the organisms given off from the noses and throats of the occupants of the operating room today is the greatest breach in so-called aseptic technic and is the cause of the majority of wound infections in well run operating rooms with a relatively good 'atraumatic technic.'

"Ultraviolet radiation (2,537 angstrom units) offers the simplest and most effective means of eliminating this source of danger and in proper intensities can be used without evident danger to the patient or to the well protected personnel.

"By this means, over a period of five years and eight months, we have secured improved wound healing, have eliminated deaths from unexplained infections in clean wounds, have reduced unexplained infections to from one-twentieth to one one-hundredth of the previous level and have secured a most gratifying reduction in both the elevation of temperature and the duration of this elevated temperature in patients following operation."

GORDON, Philadelphia.

THE USE OF SULFONAMIDE DRUGS IN BRONCHIAL ASTHMA. L. UNGER, J. Allergy **12**:528 (Sept.) 1941.

In a preliminary report on 23 cases of severe, intractable bronchial asthma treated with one of the sulfonamide drugs, choice of therapy was guided by the predominant organism found in the sputum. Sixteen patients were hospitalized;

the drug was given in doses ranging from 10 to 58 Gm., and blood concentrations of 1 to 3.8 mg. per hundred cubic centimeters were obtained. Twelve patients were treated with sulfanilamide, 9 with sulfathiazole and 2 with sulfapyridine. Only 4 of the 23 patients were improved. The remaining 19 obtained no relief.

FRIEDBERG, Chicago.

THE SPEED OF ACTION OF SO-CALLED "SLOW EPINEPHRINE" (IN OIL). L. C. BACON, M. STICKLER and R. W. LAWSON, J. Allergy **13**:48 (Nov.) 1941.

In their study of various epinephrine preparations, the authors soon noted that patients receiving ephinephrine in oil did not require preliminary doses of an aqueous preparation. It was also found that epinephrine in oil was not slow in its action, the time between administration and pharmacologic effect comparing favorably with that for equivalent doses of the aqueous preparation. Small doses of epinephrine in oil, contrary to general belief, are frequently effective.

FRIEDBERG, Chicago,

RECENT DEVELOPMENTS IN BACTERIOPHAGE THERAPY. WARD J. MACNEAL, New York State M. J. **41**:1531 (Aug. 1) 1941.

This work was carried out in the New York Post-Graduate Medical School and Hospital, Columbia University. The period between 1931 and 1940 offered 500 cases of staphylococcemia. In more than 50 of these the clinical diagnosis was thrombosis of the cavernous sinus. With bacteriophage therapy the recovery rate was 34 per cent. Twelve charts are shown in support of the conclusions, which are summarized as follows: 1. Bacteriophage is a filtrable agent of the virus group which attacks, alters or destroys bacteria under definite conditions. 2. Internally, the action is limited chiefly to holding in check organisms (staphylococci) so that intracellular and phagocytic "digestion" may take place. 3. The preparation and administration of bacteriophage for intravenous use (severe infections, such as meningitis) requires great skill. 4. When bacteriophage is thus used, low grade infections may be "rendered trivial," acute infections aborted, deep-seated lesions healed without incision or drainage and "desperate conditions heal in a surprising manner." 5. Continued administration of staphylococcus bacteriophage after active symptoms have disappeared may prevent recidivation.

In spite of this enthusiastic review, the experienced surgeon will probably wish to operate when operation seems imperative and rely on phage as an adjuvant. Sole dependence on this kind of "laboratory cure" would seem unwise, at least at present.

VOORHEES, New York.

OCCUPATIONAL ASTHMA AND VASOMOTOR RHINITIS. LOUIS STERNBERG and ALAN H. SORRELL, New York State J. Med. **41**:1649 (Aug. 15) 1941.

In the allergy clinic of Beth Israel Hospital, New York, the authors have studied workers representing a long list of occupations—bakers; furriers; metal polishers; coffee and soy, cacao and castor bean handlers; refrigerator makers; jewelers; hat makers; rag sorters; wood workers; poultry dealers; upholsterers; pharmacists and beauty parlor operators. The allergies found here were incident to inhalation, and the chief symptoms were vasomotor (nasal) or asthmatic or both. Positive cutaneous reactions are found save when the agent is a drug or a chemical. Since the latter are poor antigens, floating antibodies (reagins) are rarely found in the blood. Therefore, one may not get a positive cutaneous reaction and yet the allergy may be present. Intradermal tests may be highly dangerous, and only very small "doses" should be used. Diagnosis may depend on environment, history, microscopic study of nasal and bronchial secretions and the presence of eosinophilia. The ideal treatment is, of course, removal of the worker from his job, but this may be impossible economically; therefore tolerance

must be established. Sternberg and Sorrell take up individually the occupations mentioned, analyzing the agents inspired and citing their influence on the respiratory tract. They conclude that certain persons are "predisposed," that diagnosis is usually not difficult but is extremely important, that intradermal tests must be made with utmost caution when a drug or a chemical is concerned and that removal of the offending cause is often imperative when tolerance cannot be obtained.

VOORHEES, New York.

THE RELATIONSHIP BETWEEN DISEASES OF THE UPPER RESPIRATORY PASSAGES AND THE SURGERY OF THE CHEST. F. C. ORMEROD, J. Laryng. & Otol. **16**:277 (Aug.) 1941.

This paper is an attempt to assess the part that inflammatory conditions of the nose, paranasal sinuses and pharynx and operations on these regions play in the causation of pulmonary abscess and of bronchiectasis, and also to discuss to what extent active treatment should be applied to the nose and throat as a preliminary or as an adjuvant to surgical measures on the chest itself. The discussion is restricted to those conditions for which surgical measures become necessary and therefore does not include asthma, pneumonia or bronchitis.

Despite reasonable, and occasionally wide, differences of statistical and other data, it appears fairly well established that in about 80 per cent of cases of bronchiectasis some degree of infection of the paranasal sinuses is present and that tonsillitis plays a minor role in the causation of this disease. With abscess of the lung there is more conflict in opinion in regard to the route of infection but fairly uniform agreement that tonsillectomy is responsible in roughly 20 per cent of the cases. It is also generally admitted that general anesthesia had been used in nearly four fifths of such cases. A few cases of pulmonary abscess resulted from operation on the upper respiratory tract, but sinusitis itself did not seem to be responsible for the condition.

Infection may spread from the upper to the lower respiratory tract by aspiration, the lymph stream, the bloom stream or direct continuity. The arguments purporting to show that each of these routes is usually or often the operative factor in the development of pulmonary suppuration is freely discussed, with generous references to the literature.

If it is obvious that disease of the upper respiratory tract is a factor in the production of chronic inflammatory involvement of the lungs, the focus should be eliminated when this is possible. This is usually possible with adults, especially those with the chronic form. In children, however, since operation must be carried out under general anesthesia, the elimination of foci presents a greater problem.

LE JEUNE and BAYON, New Orleans.

Society Transactions

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

G. HENRY MUNDT, M.D., *President*

Regular Meeting, Nov. 2, 1942

Specific in Vitro Action of Sulfonamide Compounds on Pathogenic Organisms. DR. MILAN NOVAK (by invitation).

In sufficiently high concentration, such as those used in local therapy, all the common sulfonamide compounds are bacteriostatic for all species of bacteria. Specificity of drug action against a given bacterium is demonstrated only in lower concentrations, such as those obtained in systemic therapy. The choice of a sulfonamide compound for systemic therapy should be based primarily on specificity; for local treatment the accessibility of the wound and the solubility of the drug should receive the most consideration. Specificity of action as demonstrated in the test tube cannot be used as a sole criterion for selection of a sulfonamide derivative for a given condition, since toxicity, cost and relative solubility are equally important to consider.

Pharmacologic Development of the Sulfonamide Compounds and Their Action. DR. FRANK T. MAHER (by invitation).

Rational progress in chemotherapy with the sulfonamide compounds began with the development of methods of quantitative analysis, in 1937. During the past five years the importance of basic study has been increasingly evident. Controlled studies on basic properties, extensive synthesis of new derivatives, closer studies of bacterial metabolism in relation to drugs and to disease and clinical and experimental attempts to correlate the observations with factors of vital resistance have been directed toward better therapy. Of the several thousand derivatives of sulfanilamide available, only seven or eight have achieved recognition in American therapeutics.

The commonly used sulfonamide compounds may be divided into three general groups:

1. Azo derivatives of the azosulfamide (disodium-4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate) type, believed to be effective by splitting in the body to yield free sulfanilamide.

2. Compounds differing from sulfanilamide only in groupings around the sulfonamide radical, including sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole), sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) and sulfapyrazine (2-[paraaminobenzenesulfonamido]-pyrazine). These compounds offer correlated variations in pharmacologic properties, in clinical effectiveness and in toxic properties.

3. Compounds possessing more specific pharmacologic properties; this group includes sulfaguanidine (sulfanylguanidine) and succinylsulfathiazole.

Studies in experimental chemotherapy, combined with bacteriologic investigations in vitro and in vivo and extended by clinical observations, have furnished data concerning (*a*) comparative antibacterial activity, with classification of susceptible and nonsusceptible strains; (*b*) relation of species-specific variations in properties to chemical structure, which remains an empiric problem, and (*c*) comparative studies in fundamental toxicity.

Absorption studies have shown that sulfaguanidine is poorly absorbed from the intestinal tract, as is succinylsulfathiazole—thus their specificity for intestinal infection. Sulfanilamide is well absorbed from the rectum, while sulfadiazine apparently is not. Sulfathiazole does not readily pass into the spinal fluid; sulfanilamide and sulfadiazine offer advantages in this field.

All sulfonamide compounds are detoxified to a varying extent by acetylation. The acetyl derivative so formed is therapeutically inert, and conjugation therefore represents a net loss of active drug. This is particularly significant in the case of sulfapyridine, whereas sulfathiazole, sulfadiazine and sulfapyrazine have a slight loss.

Excretion of free and conjugated sulfonamide compounds occurs primarily through the urine. The irregular elimination of sulfapyridine and the rapid elimination of sulfathiazole offer significant variations for study. The excretion of these drugs into the stomach also is a factor in the nausea and vomiting which are associated with therapy with the sulfonamide compounds.

All these factors bear on concentration of the free sulfonamide compound in the appropriate body fluid. This concentration is so important that it forms the present basis for adequate dosage. Adequate levels in the blood or the spinal fluid are favored by optimal balance and uniformity in rate of absorption, distribution, detoxification and excretion.

Sulfanilamide, sulfadiazine and sulfapyrazine are absorbed and excreted at rates favoring adequate levels in the blood. Sulfadiazine and sulfapyrazine have the additional advantage of possessing the lowest level of conjugation in the group. With sulfapyridine the blood level is more difficult of maintenance. The high level of conjugation of this drug also favors the formation of urinary calculi. Sulfathiazole is rapidly absorbed and excreted; this property may make difficult the maintenance of the desired blood levels, but it may be of some advantage in cases of urinary infection, since it leads to the rapid development of high concentrations of free drug in the urine.

Urolithiasis is particularly common with the administration of sulfapyridine and sulfathiazole. Sulfadiazine and sulfapyrazine offer the seeming advantages of a lower level of conjugation; yet recent reports indicate a significant occurrence of urolithiasis with the use of sulfadiazine.

Present studies are directed toward clarification of the processes by which the sulfonamide compounds accomplish their effects and the development of derivatives possessing wider therapeutic application, with a lessened incidence of toxicity.

Clinical Experience with Sulfonamide Compounds in Otolaryngologic Practice. DR. GEORGE S. LIVINGSTON.

In otolaryngologic practice therapy with the sulfonamide compounds finds its chief value for acute infections. However, its proved effectiveness in the management of such highly fatal diseases as otitic meningitis warrants its use with less severe infections. If the sulfonamide compound is given early and in adequate dosage, the proportion of patients who fail to respond is relatively small. Late administration, the wrong choice of a drug for the particular organism causing the infection, inadequate dosage, irregular administration or an exceptionally virulent infection, with a poor immunity response on the part of the patient, may be responsible for such failures.

Sulfadiazine is at present the drug of choice. It is effective against a greater variety of organisms, is less toxic and is less likely to cause renal and other complications than are the other sulfonamide compounds, although caution must be exercised to guard against untoward reactions. A close watch must be kept on the blood count, the urinary output and the microscopic constituents of the urine, as in treatment with any sulfonamide compound. The usual indications for other measures must be heeded as they arise. Consideration must be given to the well known masking effect.

The local use of sulfonamide compounds is more satisfactory than systemic administration in certain instances. A much higher and more effective concentra-

tion of the drug can be established, with more complete bacteriostasis and less toxicity. The recent introduction of microcrystals of sulfathiazole has eliminated certain difficulties. With local administration there apparently is a tendency toward elimination of reactions of the soft tissues and toward promotion of healing and lessening of suppuration. The method is of considerable value with chronic suppuration of the sinuses but will not alone effect a cure if the pathologic process is such that surgical eradication is required.

Although the sulfonamide compounds have unquestionably proved their value, they should not be relied on solely in treatment. The proportion of complications in therapy with these substances is not large considering their widespread use, but the literature contains many reports of damage to the kidneys and blood, and a note of caution should be sounded against promiscuous and needless administration.

A résumé of my experience with acute mastoiditis at Children's Memorial Hospital is given. During 1941-1942 all patients at this hospital were treated before operation with one of the sulfonamide compounds. The use of these compounds in the mastoid cavity after operation and their employment with chronic suppuration of the middle ear and acute empyema of the maxillary sinus are also discussed.

DISCUSSION

DR. THOMAS C. GALLOWAY, Evanston, Ill.: The effect of the sulfonamide compounds on anaerobes is interesting. Fox showed that anaerobes do not respond to the use of such substances when the oxygen potential is lowered. Meleney demonstrated, however, that in the presence of zinc peroxide a good effect on these organisms may be obtained with this therapy.

Manufacturers have been saying lately that azosulfamide may be more effective than sulfanilamide. Is this so?

As much late damage has been observed to follow the use of dinitrophenol, I wonder whether Dr. Maher could give assurance that five, ten or fifteen years from now serious and irreparable changes from the use of the sulfonamide compounds may not be encountered.

It seems to me that the incidence of complications with these drugs is in an upward phase; there are now more operations on the mastoid than in the period from 1938 to 1940. In 1937, at the Evanston Hospital, my associates and I had 37 mastoidectomies, with 5 deaths; in 1938, after wide use of the sulfonamide compounds, we had 5 mastoidectomies, with no deaths. Now we are getting 10 or 12 mastoidectomies a year, with very few fatalities. I have seen 4 cases recently in which the physician had unjustified confidence in the drug, giving it for only three or four days; after preliminary recession, more stubborn infection developed, which required operation.

I have never been afraid of the masking effect. I know of no death from this cause. However, in a striking case of sinus thrombosis the symptoms of which were masked the patient did not die but had a long illness, which might have been avoided by earlier operation. One must acquire more acuity in diagnosis, so that one can allow for drug fever, simulated sepsis, etc., and when in doubt stop the use of the drug and watch the effect.

Only lately I have learned that sulfathiazole can cause persistent and troublesome hemorrhage when the microcrystals are blown between the flaps after submucous reaction.

DR. SAMUEL SALINGER: I shall comment on a limited aspect of the subject, namely, the use of sulfonamide compounds as prophylactic agents against infection. In carrying out a number of rhinoplastic procedures over a period of years, I have been confronted with a certain percentage of postoperative infections, which, though small, is distressing. The danger of infection is always present because the field, while presumably clean, is potentially infected. About a year ago I started to use sulfathiazole, giving the usual dose immediately after operation and continuing administration for four days. In checking on some 215 cases, I was surprised

to find that, despite this therapy, a pronounced reaction had occurred in 17 cases, in 7 of which pus and in 10 a serosanguineous fluid had developed. I have not had time to check on a similar series in which the drug was not used, but my recollection is that the incidence of reaction and suppuration was about the same. Also, I noted a rather high percentage of toxic reactions; in approximately 20 per cent of the series there were nausea and vomiting, occasionally so severe that the drug had to be withdrawn. I do not attribute such reactions entirely to the sulfathiazole, as all the patients received morphine and scopolamine before operation.

I must confess to some degree of disappointment in the results, although in the cases in which a serosanguineous fluid was present sulfathiazole may have prevented actual suppuration. Possibly the method of administration was faulty. At any rate, I expect to continue the use of the drug, with a closer analysis of the individual cases, and thereby obtain further information.

DR. ALFRED LEWY: The use of the sulfonamide compounds in treatment of actinomycosis has not been referred to. Cure has been attributed to their use in a number of cases. Administration apparently has not been successful when the disease affected the bone, but if the process was limited to soft tissue the sulfonamide compounds have been reported to be effective after the failure of iodides.

I was much interested in Dr. Livingston's discussion of the pros and cons of the treatment of otitis media with these drugs. He did not mention, however, that their administration has given many otologists the courage to withhold surgical treatment for a time and allow the mastoid to get well without it.

DR. JOHN R. LINDSAY: The work my associates and I carried on at the University of Chicago Clinics, and which we reported at the recent meeting of the American Academy of Ophthalmology and Otolaryngology, was confined primarily to the local use of tyrothricin and gramicidin (substances isolated from a culture of a spore-bearing soil bacillus, highly bactericidal for gram-positive micro-organisms) in the upper respiratory tract, but since we had conducted clinical investigations with the local use of sulfathiazole, sodium sulfathiazole and sulfadiazine in this area, the results with these drugs were also reported. Our experiences differed from those of Dr. Livingston. In the case of chronic suppuration of the sinuses, including the maxillary, frontal and ethmoid, we were unable to satisfy ourselves that sulfathiazole used locally after irrigation was of any definite benefit. At that time we did not have microcrystals, but we did have suspensions of finely ground sulfathiazole, in concentrations up to 30 per cent, which could be introduced through a cannula. A small amount of hydrogen peroxide was added in some cases.

In treatment of acute infection of the sinuses it may be well to remember that the suppuration is seldom limited to one sinus; there is usually more or less general infection of the upper respiratory tract, with involvement of several sinuses. Therefore the treatment, for example, of the maxillary sinus alone cannot be expected to relieve the accompanying inflammatory process in the anterior ethmoid cells or the frontal sinus, or in the upper respiratory tract in general. That appears the important reason that we did not find that the introduction after irrigation of a sulfonamide compound into the acutely infected sinuses produced any appreciable shortening of the course of the disease.

We have begun to use a 2.5 per cent solution of sulfadiazine (with triethanolamine) as a spray, as described by Dr. Crowe at the annual meeting of the American Laryngological, Rhinological and Otological Society. We have not given this drug as thorough a trial as sulfathiazole, but in our experience up to the present we have not been able to shorten the course of infection or to demonstrate any appreciable effect, as indicated by repeated cultures. This material was used in a few cases by the displacement method and produced fairly severe discomfort, lasting nearly twenty-four hours. The p_H of the solution is about 8.5, and attempts to lower the percentage of triethanolamine so as to reduce the p_H have caused precipitation.

The local use of sulfonamide compounds does have a place, however, in postoperative treatment of sinuses on which a radical operation has been performed, with removal of diseased mucosa. The effects here are similar to those in surgical wounds elsewhere, and the action in keeping down infection is unmistakable. Whether or not there is slight irritation probably is of secondary importance.

In the treatment of really severe acute sinusitis the method of choice, in our opinion, is the parenteral use of a sulfonamide compound in adequate concentration. This is the most effective way to prevent the progress and spread of such an infection. Local intervention to effect removal of a collection of pus may still be necessary, but will be rendered more safe.

DR. A. R. HOLLENDER, Miami Beach, Fla.: Irradiation is not compatible with administration of the sulfonamide compounds. I have observed 2 patients with severe toxic reactions resulting from roentgen irradiation while the drug was being taken. Radiation implies any and all sources of radiation energy, from roentgen rays to sunlight. From what I have seen, I deplore the prescribing of sulfonamide compounds for ambulatory patients. The incidence of toxic reactions is frequently increased through lack of knowledge of incompatibilities.

DR. GLENN J. GREENWOOD: I was interested in a comment I heard to the effect that a committee of the National Research Council found that the treatment of clean wounds with a sulfonamide compound caused delay in healing, as compared with the period required for controls. I have had experience in the use of solutions of these compounds in the nose comparable to that of Dr. Lindsay. In some cases the discomfort was so great that I used locally a mild anesthetic solution prior to administration of the compound. I believe that the solutions employed should be compatible, or approximately so, with the p_H of the nasal secretions. To date, in my experience, the effect of these agents in the nose has been more detrimental than advantageous.

DR. NOAH D. FABRICANT: Several weeks ago I saw a report of a number of papers given at the meeting of the American Chemical Society, one of which advanced an interesting thesis. While the discussion did not include the local application of sulfonamide compounds, it was claimed that in general the therapeutic efficacy of all such substances is definitely related to the p_H. If the drug is too alkaline or too acid, its use is undesirable, but if it is properly acid, the results are most satisfactory. I wrote to learn whether this thesis had been correctly reported, and the authors replied they would send me their observations in detail.

DR. WALTER H. THEOBALD: I should like to bear out Dr. Galloway's experience with hemorrhage. My associates and I were interested in determining whether the sulfonamide compounds would influence healing in the tonsillar fossa after tonsillectomy. The drug was used in one fossa and not in the other, which served as a control. Our observations seemed to indicate that bleeding was stimulated or promoted on the side which was treated with the drug.

DR. MILAN NOVAK: In connection with the effectiveness of treatment of actinomycosis with the sulfonamide compounds, the results of some laboratory observations may be of interest. The pathogenic actinomycetes in general are difficult to maintain in culture for more than a month, so that fresh strains must be frequently isolated from human or bovine sources (lesions of lumpy jaw in cattle). Experiments on two human strains of Actinomyces bovis and several strains isolated from the infected jaw bones of cattle showed that small quantities of the drug completely inhibited growth in the test tube. Concentrations as low as 0.5 mg. of sulfanilamide or sulfathiazole per hundred cubic centimeters were effective.

Several reports in the literature indicate that varied results are obtained in actual therapy of human infection. The probable explanation is the presence of a greater amount of purulent material in one case than in another. The effect of the sulfonamide compounds is definitely decreased in the presence of necrotic material, and much higher concentrations, of 100 mg. per hundred cubic centimeters or more,

are required to demonstrate an inhibitory effect on the organism. The logical treatment of actinomycosis, therefore, resolves itself into surgical treatment by thorough curettement, followed by local application of a sulfonamide compound to obtain a high local concentration.

DR. FRANK T. MAHER: Studies on the effect of peroxidases and oxidases go back to 1939, when Shaffer indicated that one action of the sulfonamide compounds was to inhibit certain peroxidases which break down bacteria. In a series of papers from 1939 to 1941 the inhibition of these types of enzymes was demonstrated. A year or so ago I found about fifteen theories of the mechanism of this action, among them the theory that sulfonamide compounds are effective because they inhibit catalase. That theory has fallen into disrepute at present. The investigators were not able to demonstrate the significance of inhibition of catalase in the mechanism of therapy with these substances. A number of organisms which do not come into the picture are senstive to the action of these drugs but are not peroxide producers; also, a number which produce peroxide are not particularly susceptible to sulfonamide compounds. At present the accepted theory is that of inhibition of enzymes; this concept appeared about 1938, with Lockwood's studies on the effect of peptone, extended by current studies with para-aminobenzoic acid. The defense mechanisms of the host play an important role, according to studies made by my associates and me.

Azosulfamide probably represents the last development of sulfonamide compounds of the azo type; the original group were azo derivatives, and for a time they were the only type used in practice. The French had difficulty in getting the compounds out of Germany and developed their own—diazo compounds, which are comparable to azosulfamide. There is an international variation. The action of azosulfamide is the same as that of sulfanilamide. The compound is less toxic; there is a lower incidence of nausea and vomiting; it can be used sometimes when sulfanilamide is not well received; it is more soluble, and it offers a more concentrated solution for subcutaneous or intramuscular administration. The belief exists in certain quarters that results are obtained with diazo compounds which cannot be obtained with simple sulfonamide compounds. We are not able to confirm that belief.

Botanists say that whenever a chemical drug is synthesized, there will sooner or later be some undesirable effect. That was particularly true of dinitrophenol. Such an action might be the effect of the stepping up of metabolism. The sulfonamide compounds have been employed for ten years, and in active use for five or six, and so far as I know no cases of hidden toxicity have been observed. That does not mean a toxic action may not appear.

As to the p_H, in the chemical formula for sulfanilamide the basic amino group is balanced by the acidic amido group. One German author has postulated that this chemical balance is important. Studies on urinary infections have shown that sulfonamide compounds are clinically effective at p_H levels ranging from the acid to the alkaline.

DR. GEORGE S. LIVINGSTON: The danger of the masking effect of the sulfonamide compounds is that some one not trained in observation may employ the treatment, but this should not deter one from using these substances. I feel that, although there were improvement and cessation of discharge in my cases of chronic sinusitis, I did not cure the disease. In my opinion, the sinal infection is usually complicated by some constitutional condition, especially by allergy. If one achieves favorable results, the next head cold may start suppuration again, because the membrane has never returned to normal.

As to the discomfort produced by the drug, I have had no patient complain when I used microcrystals; I have not employed a 2.5 per cent solution of sodium sulfathiazole.

There have been many recent articles for and against delayed healing with local application of the compounds. This effect may be related to a foreign body reaction in the tissues. In a recent article by Taylor (Misuse of Sulfonamide

Compounds, *J. A. M. A.* **118**:959 [March 21] 1942), it is reported that a decided reaction occurred around the site of implantation of crystals of a sulfonamide compound; other investigators have observed no reactions. Chambers reported that there was no evidence of the drug ten days after implantation. I found no difficulty with healing in the mastoid wound; with abdominal wounds the problem might be different.

As to the p_H, my only citation was that of Silcox and Schenck (Use in Otolaryngology of Microcrystals of Drugs of the Sulfanilamide Group, ARCH. OTOLARYNG. **36**:171 [Aug.] 1942), who stated that the microcyrstals have a p_H which is physiologically compatible with that of the mucosa of the respiratory tract. A recent article from the Mayo Clinic reported the use of various compounds and stated that sulfanilamide, sulfathiazole and sulfaguanidine were not hemostatic; sulfapyridine used locally was found to be hemostatic. At the Children's Memorial Hospital I used this substance routinely in the nasopharynx after adenoidectomy in about 100 cases; there was no appreciable difference in the number of postoperative hemorrhages.

I should like to emphasize sensitivity to the drug. If this proves to be a true hypersensitization, and if the increasingly widespread use of sulfonamide compounds continues, one probably can look forward to a much greater number of toxic reactions as time goes on. The literature I reviewed states that many toxic reactions are likely to occur to an increasing extent after the initial course; about 2.5 per cent of such reactions has been reported on initial administration, 36 per cent during the second course and 80 per cent during the third course of treatment. With continued repeated administration of small doses the reaction tends to be less severe.

Directory of Otolaryngologic Societies *

NATIONAL

American Medical Association, Scientific Assembly, Section on Laryngology, Otology and Rhinology

Chairman: Dr. Claude C. Cody, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. Louis H. Clerf, 1530 Locust St., Philadelphia.

American Academy of Ophthalmology and Otolaryngology

President: Dr. James A. Babbitt, 1912 Spruce St., Philadelphia.
President-Elect: Dr. Lawrence T. Post, 508 N. Grand Blvd. St. Louis, Mo.
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.
Place: Chicago. Time: Oct. 10-13, 1943.

American Broncho-Esophagological Association

President: Dr. Robert L. Moorhead, 125 Ramsen St., Brooklyn.
Secretary: Dr. Paul Holinger, 700 N. Michigan Ave., Chicago.

American Laryngological Association

President: Dr. Charles J. Imperatori, 108 E. 38th St., New York.
Secretary: Dr. Arthur W. Proetz, Beaumont Bldg., St. Louis.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. James G. Dwyer, 375 Park Ave., New York.
President-Elect: Dr. H. Marshall Taylor, 111 W. Adams St., Jacksonville, Fla.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester, N. Y.

SECTIONS:

Eastern.—Chairman: Dr. Edward J. Whalen, 750 Main St., Hartford, Conn.
Southern.—Chairman: Dr. Francis B. Blackmar, Swift Kyle Bldg., Columbus, Ga.
Middle.—Chairman: Dr. Voss Harrell, Hofman Bldg., Detroit.
Western.—Chairman: Dr. Irving M. Lupton, Medical Arts Bldg., Portland, Ore.

American Otological Society

President: Dr. Wesley C. Bowers, 17 E. 61st St., New York.
Secretary: Dr. Isidore Friesner, 101 E. 73d St., New York.

* Secretaries of societies are requested to furnish the information necessary to keep this list up to date.